بسمـــ الله الرحمن الرحيمـــ

فريق عمل كل الطب

يُقدمـــ

سلسلة كتب د/أحمد موافي

In Capsule Series

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In Capsule Series

Internal Medicine

Endocrinology

Third edition

By :

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لاَ يُكَلِّفُ اللّهُ نَفْساً إِلاّ وُسْعَهَا لَهَا مَا كَسَبَتْ وَعَلَيْهَا مَا اكْتَسَبَتْ رَبَّنَا لاَ تُؤَاخِذْنَا إِنْ نّسِينَا أَوْ أَخْطَأْنَا رَبَّنَا وَلاَ تَحْمِلْ عَلَيْنَا إِصْراً كَمَا حَمَلْتَهُ عَلَى الّذِينَ مِن قَبْلِنَا رَبَّنَا وَلاَ تُحَمّلْنَا مَا لاَ طَاقَةَ لَنَا بِه وَاعْفُ عَنّا وَاغْفِرْ لَنَا وَارْحَمْنَا أَنتَ مَوْلاَنَا فَانصُرْنَا عَلَى الْقَوْمِ الْكَافِرِينَ

صدق الله العظيم

سورة البقرة (آية٢٨٦)

Preface

- *First and foremost, thanks are due to* ***ALLAH****, to whom I relate any success in achieving any work in my life.*

- My words stand short of my supreme gratitude and thanks to Prof. Dr. ***Hossam Mowafy*** *; Head of critical care unit, Kasr El Ainy.*

*- My thanks are extended to all my medical students whom I produce this series:"****In Capsule Series****" to obtain a higher degree in internal medicine by a simple effort.*

- *Finally, I wish to thank all members of My Family, my colleagues , my Friends and even all my patients for their continuous help, encouragement and support.*

Ahmed Mowafy

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Endocrine scheme

These points should be discussed in any endocrinal disease:

1. Physiology.
2. Etiology.
3. Clinical picture.
4. Differential diagnosis.
5. Investigation.
6. Treatment.

1. Physiology : *4 items*

a. Hormone.
b. Gland.
c. **Function of the hormone**.
d. Regulation of this hormone.

2. Etiology :

a. Hyper : 👌
   i. Tumor : **adenoma**. (benign > malignant)
   ii. Hyperplasia.
   iii. Paramalignant syndrome.

b. Hypo : 👌
   i. Surgery.
   ii. Irradiation.
   iii. Tuberculosis, sarcoidosis, hemochromatosis. ♫ ♫

3. C / P :

a. C / p of the cause : e.g. pressure manifestations , tumor ….
b. C / p of the hormone :
   i. Hyperfunction = function of the hormone.
   ii. Hypofunction = opposite the function of the hormone.

N. B. Neurological manifestations : depression & polyneuropathy → may occur in any endocrinal disease.

4. Differential diagnosis : Differs according to each hormone.

5. Investigation :

a. Inv. for the cause : e.g. Imaging for the gland : U/S , CT , MRI .

b. Assay of the hormone level :

i. In blood : ↑ in hyper , ↓ in hypo

- 2 - 3 times to avoid the diurnal variation.
- It's not an ideal method because the plasma level of all hormones varies through the day (because of pulsatile secretions).

ii. In urine :

1. hormone.
2. metabolite of the hormone.

c. Investigations of the function of hormone : *see function* .

d. Dynamic test : *The principle is* :

- If a hormone level is high → suppress it.
- If a hormone level is low → stimulate it.

o **Suppression test** → for Hyperfunction.

- normal : +ve (*suppression of the hormone*)
- in this case (.....) : - ve (*no suppression*).

o **Stimulatory test** → for Hypofunction.

- normal : +ve (*stimulation of the hormone*)
- in this case (.....) : - ve (*no stimulation*).

6. Treatment :

a. Hyper :

i. Surgery.
ii. Irradiation.
iii. Medical antagonist.

b. Hypo :

i. Replacement therapy.
ii. Treatment of the cause.

Pituitary gland

- Present in Sella turcica at the base of the skull.
- Weight 0.5 gm.
- It is divided into 2 lobes :
    i. Anterior lobe.
    ii. Posterior lobe.
- Connected to the hypothalamus by the pituitary stalk.
    - Anterior lobe → connected to the hypothalamus by vascular connection
    - Posterior lobe → connected to the hypothalamus by neural connection.
- **anterior lobe :**
    - Chromophobe : non functioning (non secreting).
    - Chromophil :
        - acidophil : GH & prolactin.
        - basophile : ACTH, TSH, FSH, LH & MSH.
- **Posterior lobe :** secretes ADH & Oxytocin .

    In fact, ADH & oxytocin are synthesized in the hypothalamus & stored in the posterior pituitary .

- **<u>Regulation of pituitary hormones</u> :**

i. **hypothalamus secretes :**

- ***<u>Releasing factors :</u>*** GHRH , TRH , CRH , GnRH

- GHRH (*GH releasing hormone*) → ↑ the secretion of GH.
- TRH (*thyrotropin-releasing hormone)* → ↑ the secretion of TSH & <u>Prolactin ?</u>
- CRH (corticotropin releasing hormone) → ↑ the secretion of ACTH
- GnRH (gonadotropin releasing hormone) → ↑ the secretion of LH , FSH

- ***<u>Release inhibiting factors :</u>*** ↓ secretion of pituitary hormones.

ii. **Secretion of hormones is also regulated by -ve feedback mechanism** :

e.g. ↑ T_3 → ↓ TSH , ↑ cortisol → ↓ ACTH.

- **Function of the pituitary hormones :**
  - **GH** :
    - CHO : hyperglycemia.
    - fat : lipolysis.
    - protein : anabolic (bone, muscle & viscera)
    - minerals : ↑ all i minerals (Na, K, Ca & PO4).
  - **Prolactin** : milk secretion.
  - **FSH** :
    - ♀ → maturation of graffian follicle.
    - ♂ → spermatogenesis.
  - **LH** :
    - ♀ → ovulation.
    - ♂ → testosterone formation by the testis.
  - **ACTH** :
    - secretion of suprarenal hormones :
      - cortisone +++
      - androgen ++
      - aldosterone + (under stress only)
  - **TSH** : secretion of thyroxin by thyroid gland.
  - **MSH** : skin pigmentation.

Studying medicine without teacher is like sailing without a boat, and studying Internal medicine without **Dr/Ahmed M.Mowafy** *is like not going to the sea at all.*

Alsayed Dawoud
KasAlainy School of medicine

Acromegaly

Excessive secretion of GH in adults (after fusion of the epiphysis)

Physiology :

a. Hormone : Growth hormone (GH)

b. Gland : Pituitary gland (*anterior lobe*)

c. Function of the hormone :

i. **CHO : hyperglycemia.**

ii. **fat : lipolysis.**

iii. **protein : anabolic (bone, muscle & viscera).**

iv. **minerals : ↑ all minerals (Na, K, Ca & PO4).**

d. Regulation of this hormone :

i. ↑ GH :

1. GHRF. (*growth hormone releasing factor*)
2. hypoglycemia.
3. sleep.

ii. ↓ GH :

1. GHRIF(*growth hormone release inhibiting factor*)
2. hyperglycemia.
3. stress & exercise.

2. Etiology :

a. Adenoma.

b. Hyperplasia.

c. Paraneoplastic syndrome.

3. C / P :

a. C / p of the cause :

pressure manifestations of pituitary adenoma : visual field defect.

b. C / p of the hormone :

i. **CHO** : DM in 25 % of cases.

ii. **Fat** : excess lipolysis → loss of sc fat , wrinkling of the skin.

iii. **Protein** : excess growth of **bone**, **muscles**, **viscera**.

1. **bone :**

a. **face** : Ape like

i. **b**ig skull , enlarged nose, ears, lips & tongue.

ii. **p**rominent supra-orbital ridges & mastoid processes.

iii. **p**rognathism : prominent lower jaw with separated teeth.

iv. hypertrophy of larynx : hollow deep voice.

b. **hands & feet :**

i. spade hands & enlargement of feet.

ii. frequent change in rings & shoes.

iii. Osteoarthritis.

2. **visceromegaly** :

a. hepatosplenomegaly.

b. Cardiomegaly → congestive heart failure.

c. Endothelial hyperplasia → hypertension.

3. **muscle power** :

a. ↑↑ early. b. ↓↓ late.

iv. **Minerals** :

a. ↑ Na → hypertension.

b. ↑ K → muscle weakness , arrhythmias.

v. Neurological manifestations :

a. depression.

b. Peripheral neuropathy & carpal tunnel syndrome.

vi. Associated endocrinal manifestation :

hyperprolactinaemia & DM in 25 % of cases.

4. Investigation :

a. **Investigations for the cause** : Imaging for the gland : Skull X-ray , CT & MRI

b. **Assay of the hormone level** :

1. ↑ G.H. [normal < 5 n.gm/ml]
2. ↑ **insulin growth factor** (IGF-1 , *somatomedin*)
3. ↑ prolactin in 1/3 of cases.

*GH is difficult to measure because of its pulsatile secretions So , **insulin growth factor** (IGF-1) produced by the liver in response to GH is measured instead.*

c. **Investigations of the function of the hormone** :

i. **Blood** :

1. ↑ glucose.
2. ↑ free fatty acids.
3. ↑ Ca & ↑ P.

ii. **X-ray** :

1. skull : thick cortex , prognathism.
2. hand : tufting of the terminal phalanges (mushroom shape)

d. **Suppression test** : **glucose IV**

1. normally → +ve (↓ GH level)
2. in acromegaly → -ve (no suppression).

5. Treatment :

a. Surgery : hypophysectomy.

b. Irradiation.

c. Antagonist : Somatostatine analogue [GHRIF] : *octereotide*.

d. Symptomatic treatment : DM , Hypertension.

Gigantism

Definition : ↑↑ GH secretion before fusion of epiphysis.

C/P :

1. Generalized overgrowth of skeleton & soft tissue.
2. Disproportionate gigantism.
3. Later on features of acromegaly develops.
4. Lastly decline stage usually occurs (pituitary hypofunction)

Differential diagnosis of tall stature

1. Familial & racial : [the commonest]
2. Gigantism.
3. Excess androgen → tall children , short adult
4. 1ry hypogonadism : Disproportionate gigantism with feminine character.
5. Cerebral gigantism.
6. Marfan's syndrome.
7. Klinefelter syndrome (xxy)

First they ignore you, then they laugh at you, then they fight you, then you win.
Mahatma Gandhi

Hyperprolactinaemia

1. Physiology :

a. **Hormone :** Prolactin.

b. **Gland :** Pituitary gland [*anterior lobe*].

c. Function of the hormone : milk secretion.

d. Regulation of this hormone :

i. ↑ prolactin : PRH (prolactin releasing hormone) ?
Recently it's thought that TRH (thyrotropin releasing hormone) is a prolactin releasing hormone.

ii. ↓ prolactin : prolactin release inhibiting hormone (PRIH , dopamine)

2. Etiology :

a. Physiological : pregnancy , lactation , stress & nipple stimulation.

b. Drugs : *Antidopaminergic drugs* MCQ

i. phenothiazines. ii. methyl-dopa. iii. reserpine.

c. Pathological :

i. Pituitary : prolactinoma (*prolactin secreting pituitary adenoma*)

ii. Thyroid : 1ry hypothyroidism →↑ TRH→ ↑ prolactin.

iii. Renal : CRF → ↓ prolactin clearance.

iv. Liver cirrhosis : → ↓ metabolism.

3. Clinical picture :

a. C / p of the cause : visual disturbance due to pituitary adenoma.

b. C / p of the hormone :

i. In female :

1. glactorrhea : persistent milk production in a ♀ who is not postpartum.
2. amenorrhea.
3. osteoprosis (*due to estrogen deficiency*).

ii. In male :

1. impotence & ↓ libido.
2. infertility.
3. gynaecomastia , never glactorrhea.

4. Investigation :

a. Investigations for the cause : Pituitary imaging : X ray , CT , MRI.

b. Assay of prolactin level :

Prolactin > 300 ng/ml suggest probable pituitary adenoma. [n < 20 ng/ml]

5. Treatment :

a. Dopamine agonist :

i. Bromocriptine : 1.25 mg at bed time↑ gradually to 15 mg/d.

ii. Cabergoline : drug of choice : less side effects.

b. Surgery: for macroadenoma not responsive to medical treatment.

c. Irradiation : proton or α particles.

d. treatment of the cause : e.g. myxoedema.

Pituitary tumors

Tumor Type	Secretory Product(s)	Relative Frequency (%)
Prolactinoma (*Lactotroph Adenoma*)	Prolactin	50
Somatotroph Adenoma	Growth Hormone	10
Corticotroph Adenoma	ACTH	5
Thyrotroph Adenoma	TSH	1
Non secreting Adenoma	-----	34

Nelson's syndrome : big pituitary adenoma with very high ACTH & hyperpigmentation after bilateral adrnalectomy in a case of pituitary Cushing.

Pituitary apoplexy : sudden enlargement of the pituitary by hemorrhage into the tumor , causing combination of pressure manifestations (e.g.visual defect) & panhypopituitarism.

Panhypopituitarism in adults

(Loss of anterior pituitary function)

1. Physiology : *see before .*

2. Etiology :

a. Destruction of pituitary gland by :

i. Surgery .

ii. Irradiation.

iii. Tuberculosis, sarcoidosis, heamochromatosis.

b. Sheehan syndrome : pituitary infarction after sever postpartum hemorrhage ?

c. Neoplasm : acidophil adenoma.

d. Autoimmune.

3. C / P :

a. C / p of the cause : Surgery , Sever post-partum hemorrhage.

b. C / p of the hormones :

According to the frequency of appearance : 2 G → GH & Gondotrophins (FSH , LH) are lost early then TSH then ACTH deficiency.

i. **G**onadal deficiency :

1. ♀ : amenorrhea, ↓ libido, infertility, loss of pubic & axillary hair.
2. ♂ : impotence, ↓ libido, infertility, loss of pubic & axillary hair.

ii. **G**H deficiency : Not clinically detectable in adults , just :

1. fine wrinkles & weakness.
2. ↑↑ sensitivity to insulin (hypoglycemia).

iii. TSH deficiency : result in 2ry hypothyroidism.

iv. ACTH deficiency : Results in 2ry adrenal insufficiency it simulates Addison's disease but :

1. no pigmentation (absent ACTH)
2. no marked hypotension , due to normal aldosterone.

v. **Coma** : due to

1. hypoglycemic coma due to ↓ GH & cortisone.
2. myxoedema coma.
3. pressure in cases of pituitary tumors.

NB : *If the patient has associated DI : the problem is at the hypothalamus.*

4. Differential diagnosis :

a. From 1ry hypognadism → high FSH.

b. From 1ry Addison's disease :

c. From1ry hypothyroidism : see later

d. From anorexia nervosa :

i. normal hair & breast.
ii. aggressive attitude.
iii. normal cortisol.
iv. high GH due to hypoglycemia.

5. Investigation :

a. **Investigations for the cause :** Pituitary imaging : X-ray , CT & MRI

b. **Assay of the hormones level :**

1. ↓ GH [n : 1 – 5 n.gm/ml] & ↓ IGF-1.
2. ↓ FSH, ↓ LH & ↓ sex hormones.
3. ↓ TSH, ↓ T3 & ↓ T4.
4. ↓ ACTH & ↓ cortisol.

c. **Investigations of the function of the hormone : e.g.**

1. hypoglycemia.
2. hyponatremia.

d. **Stimulatory test :** ***insulin test***

1. In normal : +ve (↑ GH, TSH, FSH , LH & cortisol)
2. in pan-hypopituitarism : -ve (no stimulation).

6. **Treatment :**

a. Treatment of the cause.

b. Replacement therapy : *Multiple hormones must be replaced.*

i. **Hydrocortisone** : 30 mg/ d. (*20 mg a.m. & 10 mg p.m.*)

ii. Gonadal hormones : ♂ → testosterone.
♀ → estrogen / progesterone.

iii. Thyroxin : 0.1 – 0.2 mg/d , ***given after steroid replacement***.

iv. Recently :

1. purified pituitary hormones.
2. hypothalamic releasing factors.

Addiction-Free Nation Program should consider **in capsule series** its **1st** priority, as it has been proved that almost all internal medicine seekers are addicted to it.

Dr. Alsayed Dawoud
Kasr-Alainy School of Medicine

Differential diagnosis of short stature

1. **familial & constitutional : the commonest.**
2. **<u>Endocrinal</u> :**
    a. ↓ GH : Levi-lorain , Frolich's, Laurance Moon Biedle *
    b. ↓ T4 : cretinism & juvenile myxoedema.
    c. ↑ sex hormones : precocious puberty.
    d. ↑ cortisol : Cushing or excess cortisone therapy.
    e. Type 1 DM.

* *Levi-Lorain syndrome* : proportionate dwarfism , hypogonadism , normal mentality.
* *Frolich's syndrome* : trunk obesity , hypogonadism , polyphagia.
* *Laurance moon biedle* : like Frolich's + **M**R , **S**kull deformity & **r**etinitis pigmentosa.

3. **Chronic sever illness during** childhood :
    a. CVS : sever rheumatic fever, congenital heart diseases.
    b. Chest : polycystic lung disease , TB.
    c. GIT : malabsorption syndrome & malnutrition.
    d. Kidney : chronic nephritis.
4. **Skeletal causes** :
    a. Congenital :
        i. Achonrdoplasia : short limbs with normal trunk.
        ii. Osteochondrodystrophy : both limbs & trunk are short & deformed.
    b. Acquired :
        i. Rickets.
        ii. Pott's disease of spine.
        iii. Paget's disease of bone.
5. **Genetic causes** :
    a. Mongolism [Down's syndrome] trisomy 21.
    b. Turner's syndrome [45+ XO].
    c. Noonan's syndrome.

Diabetes insipidus

Deficiency of ADH

1. Physiology :

a. **Hormone :** ADH (*antidiuretic hormone , vasopressin*).

b. **Gland :** Pituitary gland (posterior lobe).

ADH is synthesized in hypothalamus & then transported along axons & stored in the posterior Pituitary.

c. Function of the hormone :

i. **↑↑ water reabsorption by collecting tubules.**

ii. **Large dose → vasoconstriction of blood vessels.**

d. Regulation of this hormone :

i. ↑↑ ADH by :

1. ↑ **osmolality**.
2. Hypovolemia & hypotension.
3. drugs : nicotine , barbiturates.

ii. ↓↓ ADH by :

1. ↓ osmolality.
2. hypertension.
3. cold weather.

2. Etiology :

a. **Central DI** : (damage of hypothalmo-hypophyseal axis)

i. **I**diopathic : most common cause

ii. **I**njury : after hypophysectomy.

iii. **I**nfection : T.B.

iv. **I**nfiltration : sarcoidosis

v. **I**nfarction : Sheehan syndrome.

vi. pituitary tumor.

b. **Familial DI** (*Walfram syndrome* , **DIDMOAD**)

hereditary condition in which there is a defect in osmo-receptrs

i. **D**iabetes **I**nsipidus.

ii. **D**iabetes **M**ellitus

iii. **O**ptic atrophy

iv. **D**eafness.

c. **Nephrogenic DI** (Renal tubules not responding to ADH)

i. Hereditary .

ii. Acquired : *MCQ*

1. renal tubular acidosis.
2. kidney amyloidosis.
3. hypercalcemia.
4. hypokalemia.
5. drugs : lithium , cholchicine.

3. C / P :

a. **C / p of the cause** : e.g. history of hypophysectomy.

b. **C / p of the hormone** :

i. **Polyuria** (up to 20 L/day) & polydepsia.

ii. Severe dehydration → weakness , weight loss & fever.

iii. Hypovitamonosis : of water soluble vitamins.

iv. Complications : shock & death.

4. Differential diagnosis : DD of polyuria. [*discussed later*]

5. Investigation :

a. **Investigations for the cause** : Pituitary Imaging : X-ray , CT & MRI

b. **Assay of the hormone level** : ↓

c. **Investigations for the function of ADH** :

i. Urine analysis :

1. Polyuria with low Specific gravity.
2. No pathological constitutes.
3. After fluid deprivation : polyuria persists.

ii. **Plasma osmolality** : ↑ due to loss of free water.

d. Stimulation tests :

i. Test the hypothalamus : ***nicotine*** test (*1-3 mg nicotine*)

1. normal : oliguria due to stimulation of ADH.
2. central DI : -ve (no stimulation)

ii. Test osmo-receptrs : IV hypertonic saline (NaCl 2.5 %) .

1. normal : oliguria.
2. osmo-receptrs defects : -ve (no olguria)

iii. **Test kidney** (**vasopressin** test) :

to differentiate between central DI & nephrogenic DI

1. in **C**entral DI : oliguria (**C**oncentrated urine)
2. in **N**ephrogenic DI : **N**o change.

6. Treatment :

a. Replacement therapy : synthetic ADH (*Desmopressine*) 20 μg/d intra nasal

b. Diet : ↓ Na , ↑ vitamins.

c. Drugs : *MCQ*

- Cholropropamide.
- Carbemazepine.
- Thiazide may be used in nephrogenic DI.

Differential diagnosis of polyuria

1. Physiological :

- Winter months.
- Excess coffee or tea.
- Diuretics.

2. Psychological : Hysterical polydepsia.

	DI	***Hysterical polydepsia***
C/P :	Polyuria then polydepsia	Polydepsia then polyuria
Fluid deprivation test :	polyuria persists	No polyuria
Osmolality	↑↑	↓↓

3. Pathological :

a. Endocrinal :

i. D.I.
ii. D.M.
iii. Adrenal : Conn's , Cushing's , Addison's.
iv. Thyroid : thyrotoxicosis.
v. Parathyroid : hyperparathyroidism.

b. Renal :

i. Nephrogenic DI .
ii. Chronic renal failure
iii. Diuretic phase of acute renal failure.

c. After any attack :

i. Migraine
ii. Epilepsy
iii. Bronchial asthma
iv. PSVT.
v. Also after the internal medicine exam. ☺

Syndrome of inappropriate ADH secretion (SIADH)

It means an excessive release of ADH

1. Physiology :

Refer to diabetes insipidus.

2. Etiology :

a. Tumors release ADH : oat cell carcinoma & lymphoma.

b. Pulmonary lesion : Legionella pneumonia , T.B.

c. CNS : meningitis, encephalitis & head injuries.

d. Drugs : **c**holropropamide , **c**arbamazepine , **c**yclophosphamide.

3. C / P :

- Increased ADH causes water retention → **dilutional hyponatremia**
  (weight gain , weakness , **c**onfusion, **c**onvulsions & **c**oma)
- No edema because of natriuresis.

4. Investigation :

1. ↓ **Na** (< 130 mEq /L)
2. ↓ serum osmolality (< 270 mosmol/kg) .
3. ↑**urine Na concentration** (> 20 mEq/L).

5. Treatment :

a. Fluid restriction → 0.8 -1 L / day.

b. demeclocycline:

   i. 600 -1200 mg /day → inhibit the action of ADH.

   ii. Given to patient unresponsive to fluid restriction.

c. For sever hyponatremia : hypertonic saline (5%) IV slowly.

Thyroid gland

Anatomy :

- The thyroid gland is located in the front of the neck below the larynx on either side of the trachea, and is formed of 2 lobes connected to each other by an isthmus. Its normal weight is about 20 – 40 gm.
- It's attached to the thyroid cartilage & to the upper end of trachea so , it moves with swallowing.

Physiology : (*hormone synthesis*)

1. **Iodine trapping :** Iodine uptake by the thyroid gland .
2. **Binding** : Tyrosine bind to iodine to form mono & di-iodotyrosine.
3. **Coupling** :
   - 2 molecules of di-iodotyrosine → T_4 (Thyroxin) : 80 mcg per day
   - Mono + di-iodotyrosine → T_3 (Tri iodothyronine) : 4 mcg per day
   - T_3 is 3-5 more potent than T_4 and acts more rapidly.
   - T_4 is converted to T_3 in the peripheral tissue.
4. **Release** :
   - T_3 & T_4 release under the control of TSH.
   - Thyroid hormones circulate in 2 forms :
     - ✓ Protein bound, mainly *thyroxin binding globulin* (TBG): > 99 %
     - ✓ Free part (active part) : less than 1 %

Thyroid diseases

Causes of thyrotoxicosis :

1. **Toxic diffuse goiter :** *The commonest cause*
   (Grave's disease in USA, Basedow's disease in Europe).
2. **Toxic nodular goiter.**
3. **Toxic solitary adenoma.**
4. Excess production of TSH by pituitary tumor (very rare).
5. Extrathyroid source of hormone :
   a. Thyrotoxicosis factiscia : exogenous intake of thyroxin.
   b. Ectopic thyroid tissue e.g. strauma ovarii .
6. Iatrogenic : amiodarone.

Classification of hypothyroidism :

- According to the age of onset :
  1. Cretinism : during infancy.
  2. Juvenile myxoedema : before puberty.
  3. Myxoedema : after puberty.
- According to the site of the cause :
  1. 1ry hypothyroidism : cause in the thyroid gland.
  2. 2ry hypothyroidism : cause in the pituitary gland.
  3. 3ry hypothyroidism : cause in the hypothalamus.

1ry thyrotoxicosis
(*Grave's disease*)

Autoimmune disorder consists of :

- Hyperthyrodism *plus* one or more of the following triad
- Painless diffuse goiter (90 %)
- Ophthalmopathy (60 %)
- Dermopathy. (2 %)

1. Physiology :

a. Hormone : T3 & T4 .

b. Gland : Thyroid gland.

c. Function of the hormone : *Hormone of metabolism*

i. stimulate physical , mental & sexual growth.
ii. ↑ energy production & O_2 consumption.
iii. ↑ glucose absorption & uptake by cells.
iv. ↓ cholesterol level.
v. ↑ the respiratory & heart rate.
vi. stimulation of erythropoiesis (↑ RBCs).
vii. ↑ the tissue responsiveness to catecholamine.
viii. Hepatic conversion of carotene to vitamin A .

d. Regulation of this hormone :

i. TSH. ii. TRH.

2. Etiology :

Autoimmune disorder in which there is Formation of auto antibodies (***T****hyroid* ***s****timulating* ***i****mmunoglobulin* - TSI) that bind to and activate the thyroid TSH receptors .

3. Clinical picture : (♀ 30 – 40 years).

a. C / p of the cause :

Association of autoimmune diseases as myasthenia & DM.

b. **C / p of the hormone** :

General :

- polyphagia with loss of **w**eight.
- intolerance to hot **w**hether.
- progressive muscle **w**eakness.

GIT :

- ↑↑ appetite (with loss of weight).
- diarrhea.
- Just palpable spleen.

Genital :

- ♀ : amenorrhea.
- ♂ : Impotence & gynaecomastia.

Cutaneous :

- skin is thin ,warm & flushed with generalized sweating.
- hair : fine & thin.
- nails : clubbing of fingers. (*Thyroid acropachy*)
- **preitibial myxoedema** : (*dermopathy*)

irregular, **i**tchy, tender& hairy swelling over the chin of the tibia & usually symmetrical, due to deposition of mucin-like substance in the S.C. tissue.

CVS : (more common in *older* patients)

1- pulse :

- **rate** : ↑ , the sleeping pulse rate is usually > 100 b/m .
- **rhythm** : may be irregular due to AF or extrasystole.
- **character** : water hummer pulse due to big pulse volume.
- **equality** : unequal on both sides → retro-sternal goiter.

Thyroid function tests are mandatory in any patient with atrial fibrillation

2- heart : Hyperdynamic circulation ⇨ volume overload ⇨ cardiac enlargement then heart failure.

3- Blood Pressure :

- systolic : ↑ (isolated systolic hypertension)
- diastolic : ↓ (thyroxin → VD)

So, there is big pulse volume

CNS : (more common in *younger* patients).

- **psychic :** 4 *mnemonic* : naim
  - **n**ervousness.
  - **a**nxiety & **a**gitation.
  - **i**nsomnia.
  - **m**ental disturbance.
- **organic :** 4
  - fine tremors in tongue & hands.
  - polyneuropathy.
  - myopathy.
  - myasthenia.

It's important to note that elderly patients with hyperthyroidism may be lethargic rather than agitated (***apathetic thyrotoxicosis***).

Eye :

1. Exophthalmos :

- bilateral , but may start unilateral.
- May occur even before the appearance of thyrotoxicosis.
- AE: oversecretion of autoantibody called **exophthalmos producing substance (EPS)** ⇨ lymphocytic **infiltration** of retrobulbar tissue & extrinsic muscles.
- Blindness may occur secondary to corneal ulcers or optic nerve compression.

2. certain eye signs : (*DR must be very simple*)

a. **D**alrymple's sign (*Lid retraction*) : rim of sclera is seen between the cornea & upper lid.

b. **R**osenbach's sign : fine tremors of eyelids on slight closure of eye.

c. **M**oebius' sign : lack of convergence due to weak medial recti muscles.

d. **V**on-Grave's sign : lid lag on looking down.

e. **S**tellwag's sign : infrequent blinking.

N.B: ocular manifestations can be divided into 2 types:

- ✓ **Infiltrative ophthalmopathy** (mechanical , due to accumulation of autoantibodies) e.g. exophthalmos & mobius sign → so both are specific to Grave's disease.
- ✓ **Non- Infiltrative ophthalmopathy** (due to ↑ thyroxin) e.g. lid lag, lid retraction , stellwag & Rosenbach's sign → occur with any thyrotoxicosis (*not specific to Grave's disease*).

Gland :

a. Inspection : mild to moderate enlargement of the gland.

b. Palpation : - consistency : fleshy or firm. – surface : smooth.

c. Percussion : dullness over manubirum-sterni in retro-sternal extension.

d. Auscultation : systolic bruit may be heard due to high vascularity.

Thyrotoxic crisis (*thyroid storm*):

- an extreme form of thyrotoxicosis with a mortality of 10 %.
- it's precipitated by stress (acute illness , surgery) or infection.
- it's considered one of the medical emergencies.
- **C/P :** sever manifestations of thyrotoxicosis that include :
  a. general : fever > 41˚C.
  b. C.V.S. : sever tachycardia, acute HF & AF.
  c. C.N.S. : marked irritability, mental disorientation & coma.

Differential diagnosis :

a. *Neurosis* : → cold hand & normal sleeping pulse.
b. ↑*appetite with loss of weight*: DM , parasitic infection.
c. *Hyperdynamic circulation.*
d. *Muscle diseases* : myopathies, myasthenia gravis.
e. **Difference between 1ry & 2ry thyrotoxicosis** :

	1ry thyrotoxicosis	*2ry thyrotoxicosis*
- **Other name :**	Grave's disease.	toxic multi nodular goiter.
- **Cause :**	Auto-immune.	On top of nodular goiter.
- **Age of onset :**	30 – 50 year.	50 year.
- **Thyroid gland :**	Diffusely enlarged.	Nodular.
- **CVS :**	Mild.	Sever.
- **CNS :**	Sever.	Mild.
- **Exophthalmos :**	Present.	Absent.
- **Monosymptomatic cases:**	Un-common.	Common.
- **TTT :**	Usually medical.	Usually surgical.

monosymptomatic cases : when one of the manifestations of thyrotoxicosis predominates e.g. *thyrocardia* : cardiac symptoms only (AF) .

Investigation : (*Thyroid function tests*)

I. **Investigations for the cause** :

1. TSH level : [n = 0.5 – 5 µu/L]
   a) It's the **most sensitive** test of thyroid function.
   b) ↓↓ in most cases of thyrotoxicosis by –ve feed back mechanism.
   c) ↑↑ only in **TSH producing pituitary tumor** : very rare.
2. Imaging for the gland :
   a) thyroid scan :
      - hot nodules : benign.
      - cold → do U/S.
   b) U/S : indicated in cold solitary thyroid nodule :
      - cystic → benign.
      - solid : malignant → do *needle aspiration biopsy*.
3. Thyroid receptor antibodies : thyroid stimulating immunoglobulin (TSI) can be detected in Grave's disease.

The term LATS (long acting thyroid stimulator) referring to this antibody is no longer used.

II. **Assay of the hormone level** : 6

a) Total T3 ↑↑ : [n : 70 – 170 ngm%] → not accurate.

b) Total T4 ↑↑ : [n : 5 – 12 µgm%] → not accurate.

T3 & T4 are over 95% protein bound to TBG (thyroxin binding globulin) so,....
o Increased TBG as in pregnancy → ↑↑ total T3 & T4 but free T3 & T4 are normal.
o Decreased TBG as in liver cirrhosis & nephrotic syndrome → ↓ total T3 , T4 but free T3 , T4 are normal.

c) **free T3** (n : 0.4 ng %)

d) **free T4** (n : 1.6 ng %) difficult to measure , we use free T4 index.

e) T3 resin uptake : ↑

Radioactive T3 is added to the patient's serum it's fixed to the unoccupied binding sites of TBG → the remaining radioactive is then absorbed into a resin (n = 25% - 35%).

f) free thyroxin index : ↑ (> 11.5) = T3 resin uptake x total T4.

III. Investigations for the function of the hormone :

- Blood :
  - ✓ ↓ cholesterol , ↑ Ca , ↑ Calcitonin in medullary carcinoma.
  - ✓ Lag sugar curve.
- Urine : Polyuria , ↑ glucose.

IV. Suppression test : material : **T3** .

- ✓ Normally → ↓ RAIU (*radio active iodine uptake*).
- ✓ in thyrotoxicosis → no effect.

Treatment :

I. Medical :

Indication :

- 1ry thyrotoxicosis (Grave's disease).
- 2ry cases : pre-medication before operation.
- Treatment of complications e.g. HF.
- pregnancy.

Contraindications :

- huge goiter.
- retro-sternal goiter.
- suspicion of malignancy.

Lines of medical treatment :

- **β-blockers** e.g. propranolol to provide rapid symptomatic control.
  They also decrease peripheral conversion of T4 to T3.
- **Anti-thyroid drugs** :
  - methyl thiouracil : **200**mg t.d.s. then reduce after 4-6 w to **100** mg t.d.s.
  - propyl thiouracil : **100**mg t.d.s. then reduce after 4-6 w to **50** mg t.d.s.
  - Carbimazol (Neomercazol): **20** mg t.d.s. then reduce after 4-6 w to **10** mg t.d.s
    - Duration : 1 - 2 years. (*until thyroid hormone stores become depleted*)
    - Mechanism : These drugs inhibit the formation of thyroid hormones.
      Propylthiouracil : also inhibits conversion of T4 to T3.

- Side effects :
  - ✓ Allergy .
  - ✓ Agranulocytosis .
  - ✓ Hypothyroidism.
  - ✓ Goiter : due to ↑ TSH.
  - ✓ Relapse : on sudden stoppage.
  - ✓ Others : GIT upset, cholestatic jaundice .

II. Radio-active iodine :

Indication :

- ✓ failure of medical treatment.
- ✓ patient is unfit for surgery.
- ✓ recurrence after thyroidectomy.
- ✓ toxic adenoma.

Contraindications :

- ✓ during pregnancy, lactation & childhood.
- ✓ huge goiter & retro-sternal goiter.

Side effects :

- ✓ hypothyroidism.
- ✓ bone marrow depression.
- ✓ fetal anomalies, if taken in pregnancy.
- ✓ ↑ incidence of malignancy, so → not given in childhood.

Precautions :

It's important to stop anti-thyroid drugs 4 days before & 4 days after radioactive iodine therapy as it prevents radioactive iodine uptake by the gland.

III. Surgical : (*sub-total thyroidectomy*)

Indication :

- ✓ 2ry thyrotoxicosis.
- ✓ failure of medical treatment in 1ry case of young age.
- ✓ huge or retro-sternal goiter.
- ✓ suspicion of malignancy.

Pre-operative preparations :

Lugol's iodine (*5% iodine in 10% K iodide*) : ↓ size & vascularity of the gland.

Complications :

Laryngeal nerve palsy , transient hypocalcaemia , hypothyroidism.

IV. Treatment of complications :

- **Ocular complications :**
  - ✓ protect eye by ointment, sun glasses.
  - ✓ prednisone → ↓↓ lymphocytic infiltration.
  - ✓ radiotherapy of the orbit. ✓ orbital decompression.
- **Heart failure :**
  - ✓ bed rest, salt restriction, digitalis & diuretics.
  - ✓ persistence of AF → Digitalis or DC shock
- **Preitibial myxoedema :** local Betamethasone cream (local steroid)
- **Thyrotoxic crisis : 6**

1. **p**ropranolol in full dose is started immediately for tachyarrhythmias
   (1 mg every 5 min IV until the desired effect is achieved then 20 - 120 mg/6h orally)
2. **p**ropylthiouracil : 100 mg/8h. (orally, rectally or nasogastric tube).
3. Na iodide: *1 gm over 24h IV* → ↓↓ thyroxin release from thyroid gland.
4. hydrocortisone : 100 mg/8h IV , to correct the hypotension.

> - *Thyrotoxic crisis → ↑↑ cortisol metabolism → relative adrenal insufficiency → refractory hypotension*
> - *Hydrocortisone correct this hypotension. Also, steroids prevent peripheral conversion of T4 → T3*

5. Treatment of precipitating factor : antibiotics for infections.
6. symptomatic treatment :
   - hyperthermia : ice bags.
   - dehydration : IV fluid.

Thyrotoxicosis in pregnancy :

- ✓ Medical treatment : **p**ropyle thio-uracil.
- ✓ Radioactive iodine : absolutely contraindicated as it is teratogenic & carcinogenic
- ✓ Surgery indicated in : appearance of side effects.
- ✓ Follow up: should be done to diagnose neonatal thyrotoxicosis because TSI can cross the placenta & stimulate fetal thyroid gland.

Myxedema

(Hypothyroidism in adult)

1. Physiology :

Refer to hyperthyroidism.

2. Etiology & types :

a. 1ry mxyedema : (5 **I** + **H**)

i. **I**diopathic atrophy of the gland.

ii. **I**atrogenic :

1. post thyroidectomy.
2. radioactive iodine.
3. anti-thyroid drugs.
4. lithium.
5. amiodarone.

iii. **I**nfections : viral infection (De Quervain's thyroiditis)

iv. **I**odine deficiency.

v. **I**nfiltration : tumor.

vi. **H**ashimoto's thyroditis :

1. auto-immune disease. (thyroid antibodies : +ve).
2. gland is replaced by lymphocytic infiltration.
3. gland is firm, symmetrically enlarged & not tender.
4. transient thyrotoxicosis may occur followed by hypothyroidism.

b. 2ry Myxedema : 2ry to pituitary failure e.g. tumor (↓ TSH).

c. 3ry myxedema: deficiency of TRH secreted from hypothalamus.

d. Peripheral resistance to thyroid hormone : very rare .

3. Clinical picture : ♀ > ♂ *30 – 50 years.* ☺

a. C / p of i cause : Surgery , Anti-thyroid drugs.

b. **C / p of i hormone** :

In hypothyroidism every thing slows down except the period !!

i. **General** :

1. intolerance to cold.
2. lethargy & fatigue.
3. weight gain.
4. serous effusions (pleural , pericardial & ascites).
5. face :
   a. expressionless.
   b. puffy eye lids.
   c. loss of outer 1/3 of eye brows.
   d. large tongue.

ii. **GIT** :

1. **slow** motility → constipation
2. **slow** absorption → malabsorption syndrome.

iii. **Genital** :

1. ♀ → **menorrhagia.**
2. ♂ → impotence & gynaecomastia.

iv. **Cutaneous** :

1. dry, cold, pale & non sweaty skin.
2. non pitting edema : due to intradermal accumulation of proteins, not interstitial edema fluid.
3. yellowish discoloration due to carotinemia.
4. hair loss.

v. **CVS** :

1. hypercholesterolemia → ischemic heart disease.
2. diastolic HTN due to ⇩ thyroxin (thyroxin ⇨ VD)
3. sinus bradycardia.
4. Pericardial effusion.

vi. **CNS** :

1. **slow** intellectual & motor activity.
2. deposition of mucopolysaccharide in :
   a. tongue : **slow** speech.
   b. vocal cords : hoarseness of voice.
   c. flexor retinaculum : carpal tunnel syndrome.
   d. peripheral nerves : peripheral neuropathy.
   e. joints & muscles : **slow** relaxed reflexes.

vii. **Heamatological** :

1. normocytic normochromic anemia : BM inhibition.
2. microcytic hypo-chromic anemia : menorrhagia.
3. macrocytic :associated pernicious anemia (12%)

viii. **Hypothyroid coma** (***Myxedema coma***) :

1. untreated long standing hypothyroidism.
2. precipitated by cold exposure or infections.
3. manifested by : **5 H**
   a. **H**ypothyroidism with loss of consciousness.
   b. **H**ypothermia. c. **H**ypoglycemia.
   d. **H**ypoventilation (respiratory depression).
   e. **H**eart failure.

Although this condition is called Myxedema coma , frank coma is uncommon !!

ix. **Gland** :

1. ↑ size as → Hashimoto's thyroditis.
2. atrophy → 1ry idiopathic forms.
3. scars of previous operations.

4. Differential diagnosis :

a. Nephrotic syndrome.

b. Depression.

c. Other causes of hypothermia : cold weather , shock , Addison's disease , hypoglycemia.

d. Difference between thyroid & pituitary myxedema :

	Pituitary myxedema	**thyroid** myxedema
1. Clinical picture :		
a- Of thyroid :		
▪ Dry skin puffy lid :	- Not marked	- Marked
▪ Body weight :	- ↓↓	- ↑↑
b- Of hypogonadism	- Marked	- Absent
2. Investigation :		
a- TSH :	- Low	- High
b- FSH/LH :	- Low	- Normal
c- ACTH, Cortisol :	- Low	- Normal

5. Investigation :

a. Investigations for the cause :

i. **TSH** : [**test of choice**]

↑↑ in thyroid myxedema , ↓↓ in pituitary myxedema.

ii. Thyroid antibodies.

b. Assay of the hormones level :

1. serum hormones :
   a. TSH : ↑↑ in 1ry type. [test of choice]
   b. T4 & T3 : ↓↓

It is important to note that normal T4 not exclude hypothyroidism

2. radio-active iodine uptake : ↓

c. Investigations of the hypofunction of thyroid hormone :

i. Blood :
   1. CBC : anemia
   2. blood glucose → flat sugar curve.
   3. ↑ cholesterol.
   4. ↑ CPK (creatinin phospho-kinase).
   5. ↑ LDH (lactate dehydrogenase).

ii. ECG findings : sinus bradycardia , low voltage.

iii. BMR : low.

DD of low voltage ECG :

- Hypothyroidism.
- Pericardial effusion.
- Obesity.

6. Treatment :

a. **Replacement therapy** : life long

- L-thyroxin : start small dose 0.05 mg/d & gradually up to maintenance dose (0.2 – 0.3 mg/day).
- The dose is increased very gradually to avoid precipitation of angina & HF .

b. **Treatment of myxedema coma :** 6

a. **Hypothyroidism** : T3 : 5 µg/8h IV.

b. **Hypothermia** : gradual rewarming.

c. **Hypoglycemia** : glucose IV.

d. **Hypoventilation** (respiratory depression) : O2 & ventilation.

e. **Heart failure :** cardiac support.

f. **Treatment of precipitating factors** e.g. antibiotics for infections.

Goitre

Definition : Enlargement of the thyroid gland.

classification:

i. Simple goitre : (non toxic , non inflammatory , non neoplastic)

Persistent low level of thyroid hormones → ↑ TSH → thyroid enlargement.

- **P**hysiological : **P**uberty , **P**regnancy. *(due to increased the demond of iodine, so there is relative iodine deficiency)*
- Iodine deficiency.
- Drugs : Anti-thyroid drugs , lithium.

ii. Toxic goitre : *(goitre with hyperthyroidism)*

- Diffuse : Grave's disease (1ry thyrotoxicosis)
- Toxic nodular goitre (2ry thyrotoxicosis , Plummer's disease)

iii. Inflammatory goitre : e.g. Hashimoto's thyroiditis .

iv. Neoplastic goitre .

Cretinism

Hypothyroidism during infancy

1. **Physiology :** Refer to hyperthyroidism.

2. **Etiology :**
   a. Congenital.
   b. Endemic cretinism → iodide deficiency.
   c. Excess anti-thyroid drugs during pregnancy.

3. **Clinical picture :**
   a. Persistent physiological jaundice.
   b. Hoarse cry & feeding problems.
   c. Disproportionate dwarfism.
   d. Big lips & protruding tongue & Delayed dentation.
   e. Delayed walking.
   f. Muscle weakness(*pot belly with umbilical hernia*).
   g. Dry & cold skin.
   h. Mental detoriation if not treated within 6 months.

4. **Investigation :**
   a. T4 & T3 : ↓↓
   b. TSH : ↑↑
   c. X-ray of carpal bone : delayed appearance of ossification centers

5. **Treatment : Replacement therapy**
   - L-thyroxin 0.025 mg/day & ↑↑ dose up to 0.2 mg/day
   - It should be started before the 1st 6 months to avoid mental retardation.

Parathyroid gland

Ca metabolism

- Normal Ca level : 8.5 – 10.5 mg%.

A. **Ionized** (*active*) : 50%

B. **Non-ionized** (*reserve*) : 50%

- 40% bound to albumin. - 10% any other bond (Ca carbonate, phosphate ....)

Liver cirrhosis & nephrotic syndrome → ↓ albumin → hypocalcaemia , but no tetany because ionized Ca is still normal.

- Regulation of Ca :

- Ca level is closely affected & related to P [n. 3 - 4.5 mg%]
- Notice that Ca X P = constant [40].
- Serum Ca & P levels are controlled by certain hormones :
  a. Parathormone.
  b. Calcitonin.
  c. Active vitamin D.
- Ca regulation involves 3 sites : bone, intestine & kidney.

	Parathormone*		***vitamin D***		***Calcitonin***	
Absorption (intestine)	↑ Ca	↓ P	↑ Ca	↑ P	↓ Ca	
Reabsorption (kidney)	↑ Ca	↓ P	↑ Ca	↑ P	↓ Ca	↓ P
Resorption (bone)	↑ Ca	↓ P	↑ Ca	↑ P	↓ Ca	↓ P
Blood (net result)	**↑ Ca**	**↓ P**	**↑ Ca**	**↑ P**	**↓ Ca**	**↓ P**

*PTH acts directly on bone & kidney & indirectly on intestine (through activation of vit.D).

Hyperparathyroidism

1. Physiology :

a. Hormone : Parathormone (PTH)

b. Gland : Parathyroid gland.

c. Function of the hormone : ↑ Ca , ↓ P

- **i.** GIT : ↑↑ *absorption* of Ca.
- **ii.** Kidney : ↑↑ *reabsorption* of Ca.
- **iii.** Bone : ↑↑ *resorption* of Ca.
- **iv.** ↑ Renal Phosphate excretion.

d. Regulation of this hormone :

hypo Ca or **hyper P** → ↑ PTH .

2. Etiology :

a. 1ry :

- **i.** Adenoma of the parathyroid gland. *(most common)*
- **ii.** Hyperplasia of the parathyroid gland.
- **iii.** As a part of **M**ultiple **E**ndocrine **N**eoplasia (MEN - 1) : 3 **p**
  1. hyper-**p**arathyrodisim.
  2. **p**ituitary tumor.
  3. **p**ancreatic tumor.

b. 2ry :

Due to prolonged ↑ **P &** ↓ **Ca** as in **Chronic renal failure** which leads to hyperplasia of the parathyroid gland.

c. 3ry : usually in end stage CRF

- Longstanding 2ry hyperparathyroidism → irreversible parathyroid hyperplasia . (start 2ry → end 1ry)
- Parathyroidectomy is the only appropriate treatment.

d. Paramalignant syndrome (*oat cell carcinoma*).

3. C / P : 50% → asymptomatic.

a. C / p of the cause : parathyroid adenoma , CRF.

b. C / p of the hormone : ***disease of bone & renal stone*** ♫♫

i. **Bone** : (2)

1. **p**ain.
2. **p**athological fracture.

ii. **Renal** : (3)

1. repeated **stones.**
2. polyuria (Ca diabetes) & polydepsia.
3. nephrocalcinosis with renal failure may occur.

iii. **Others** : (4) X 2

1. **CNS** :
   a. drowsiness.
   b. depression.
2. **GIT** :
   a. peptic ulcer.
   b. pancreatitis (**abdominal pain**).
3. **CVS** :
   a. ECG : short Q-T interval & arrhythmia.
   b. Hypertension.
4. **Skin** :
   a. dry.
   b. itching.

- Ca > 11mg%. → Clinical manifestations of Ca
- Ca > 13mg%. → Renal impairment
- Ca > 14 mg% → Coma & cardiac arrest (*endocrinal emergency*)

4. D. D. of hypercalcemia : (4 X 3)

a. Endocrine :

i. Hyperparathyroidism (1ry & 3ry). **The most common cause**

ii. Hyperthyroidism.

iii. Addison's disease (Cortisone → -- vit.D).

b. Malignancy :

i. Bronchogenic carcin*oma* .

ii. Multiple myel*oma*.

iii. Lymph*oma* → activation of vitamin D .

c. Bone :

i. T.B.

ii. Sarcoidosis.

iii. Immobilization.

d. Others :

i. Hypervitaminosis (vitamin D).

ii. Drug induced : thiazide , lithium.

iii. Familial hypocalciuric hypercalcemia.

5. Investigation :

a. **Investigations for the cause :** Parathyroid imaging: CT, MRI , radioisotope scan

b. **Assay of the hormone level** : parathormone : ↑↑ [n: 0.5 – 1 ngm/ml]

c. **Investigations of the function of the hormone :**

i. Blood :

	1ry	2ry	3ry
1. Ca	↑	↓	↑
2. P	↓	↑	↑
3. Alkaline phosphatase	↑	↑↑	↑↑↑

NB : *Persistent hypercalcemia , hypo P & an elevated PTH confirm the diagnosis of 1ry hyperparathyroidism.*

ii. Urine :

1. ↑ Ca [n : 150 mg / day]
2. ↑ P [n : 1 gm / day]
3. ↑ hydroxyproline & c-AMP due to ↑ bone resorption.

iii. X- ray :

1. bone :

a. **loss of lamina dura of the teeth. (*the earliest sign*)**
b. sub-periosteal erosions in the middle phalanges.
c. ground glass appearance of the bones.
d. skull → mottling of the skull. (*salt & pepper skull*).
e. spine → cod fish spine (indentation of vertebrae by discs)

2. renal : urinary stones , nephrocalcinosis.

iv. *Bone biopsy :* osteomalacia with excess osteoclasts.

d. <u>Suppression test :</u> (***<u>steroid test</u>***)

i. +ve (↓ Ca level) → normal.
ii. –ve (no suppression) → Hyperparathyroidism.

6. <u>Treatment :</u>

a. Surgery :

i. Removal of the parathyroid glands.
ii. Ca & vitamin D supply to avoid tetany.

b. Medical treatment of hypercalcemia :

i. ↓ intake & ↑↑ fluid intake.
ii. ↓ absorption : by oral phosphate.
iii. ↑ loss of Ca : saline then fursemide or dialysis in sever cases.
iv. Calcitonin .
v. β-blocker : ↓ the adverse effect of hypercalcemia on the heart
vi. Cortisone is effective in some cases (vit.D excess & sarcoidosis)
vii. Alendronate (Osteomax) : ↓↓ osteoclastic activity.

Hypercalcemic crisis (serum Ca level > 14 mg %)

a. **Manifestations** (*non secific*) :

i. *GIT* : Nausea , vomiting ,constipation & abdominal pain.
ii. *Renal* : Polyuria & dehydration.
iii. *CNS* : Confusion & coma.
iv. *CVS* : Arrythmia , shortened QT interval.

b. Treatment :

i. **IV normal sline** : 4-6 L/day may be nessary. (the first goal)
ii. **Lasix** (40 – 80 mg IV every 2 hours) , but be sure that the patient is adequatly hydrated.
iii. IV pamidronate (*Aredia*) : drug of choice.
iv. Calcitonin : it inhibits bone resorption.
v. Cortisone.
vi. Dialysis is effective in removing Ca in patients with renal failure.



ديناصور الطـــــــب المنقرض

Hypoparathyroidism

(Tetany)

Definition of tetany :

state of ↑↑ neuro-muscular irritability due to: ↓ ionized Ca , ↓ Mg or alkalosis.

Etiology of tetany : (↓ ionized Ca , ↓ Mg or alkalosis)

a. **Hypocalcaemia** :

i. Hypoparathyroidism :

1. surgery removal.
2. irradiation.
3. Di- george syndrome : absent parathyroid & thymus glands.

ii. ↓ Ca intake : starvation.

iii. ↓ Ca absorption :

1. malabsorption syndrome.
2. ↓ active vitamin D.

iv. Precipitation of Ca in tissue e.g. acute pancreatitis.

v. ↑ Ca excretion : **CRF (most common cause of hypocalcemia**).

N.B. tetany rarely occurs in RF because of acidosis which convert non ionized Ca into ionized Ca.

b. **Hypomagnesaemia** : Excess diuretic , Malabsorption syndrome.

c. **Alkalosis** : (**Ionized Ca → non ionized Ca**).

i. Respiratory alkalosis : any case of hyperventilation :

ii. Metabolic alkalosis :

1. loss of HCl : vomiting , gastritis , gasterectomy.
2. milk alkali syndrome.
3. hypokalemia e.g. Conn's syndrome.

*hypokalemia (**K loss**) ⇆ Al-**K**-**Loss**is ☺*

C / P of Tetany :

iii. **Latent tetany :** **(serum Ca = 7 – 9 mg%)**

1. manifestations of tetany are not present.
2. manifestations appear by *provocative tests* :
   a. **Chvostek's test :**
      tapping over the facial nerve → contraction of the facial muscles.
   b. **Trousseau's test :**
      Inflation of a BP cuff above SBP for 3 minutes → carpal spasm.
   c. **Erb's test :** (normally : 8 mili-ampers at least are needed for stimulations)
      electric current < 4mili-ampers → muscle contraction.

iv. **Manifest tetany : (serum Ca < 7 mg%)**

1. irritability & parasthesia around mouth & fingers.
2. muscle twitches & may be convulsion in severe cases.
3. spasm :
   a. eye lids : blepharospasm.
   b. mouth : trismus of jaw.
   c. larynx : laryngospasm.
   d. **carpo-pedal spasm**.
   e. diaphragm : Hiccough.
   f. GIT : abdominal colic.
4. Cardiovascular : QT prolongation , refractory HF , hypotension.
5. on ectodermal structures : (*only in hypocalcemia*)
   brittle nail , hypoplastic teeth , cataract.

Investigation : (for the cause)

- In hypoparathyrodism : ↓ PTH , ↓ serum Ca , ↑ P.
- In hypomagnesaemia : **Refractory hypokalemia**. **MCQ**
- In alkaosis : ↑ PH , ↓ ionized Ca.

Treatment :

a. Acute attack : IV **Ca gluconate** 10 ml 10% very slowly.

b. Treatment of the cause :
   - Hypocalemia : oral Ca , vitamin D
   - Hypomagnesemia : oral Mg.
   - Alkalosis : Treatment of the cause , acidifying drugs.

Suprarenal gland

(Adrenal gland)

- There are 2 adrenal glands at the superior pole of each kidney.

- They are composed of outer cortex & inner medulla :

i. Adrenal cortex (*the outer part*) which is formed of 3 separate layers :
   - Zona **G**lomerulosa : secretes aldosterone (*mineralocorticoids*).
   - Zona **F**asciculata : secretes cortisol (*glucocorticoids*)
   - Zona **R**eticularis : secretes androgen.

ii. Adrenal medulla (*the inner part*) : secrets catecholamines.

Disorders of suprarenal gland :

- **Hyperfunction of adrenal cortex :**
  - Conn's syndrome : ↑ aldosterone.
  - Cushing syndrome : ↑ Cortisol.
  - Adrenogenital hyperplasia : ↑ androgen.
- **Hyperfunction of adrenal medulla :** Pheochromocytoma.
- **Adrenal cortical hypofunction :** Addison's disease (1ry adrenal failure)

Conn's syndrome

(1ry hyperaldosteronism)

1. Physiology :

a. **Hormone** : Aldosterone.

b. **Gland** : Suprarenal gland (*Zona glomerulosa*).

c. **Function** :

i. **↑ Na , ↑ H_2O.**

ii. **↓ K , ↓ H^+.**

d. **Regulation** : Aldosterone secretion is stimulated by :

i. Hypovolemia → **↑ Renin** → ↑ aldosterone

ii. ↑ K (hyperkalemia)& ↓ Na (hyponatremia)

iii. A.C.T.H. → during stress only.

2. Etiology :

a. Adenoma of zona glomerulosa.

b. Hyperplasia of zona glomerulosa.

c. Paraneoplastic syndrome.

3. Clinical picture :

a. **C/p of the cause** : Adenoma , Paraneoplastic syndrome ….

b. **C/p of the hormone** : (↑ Na , ↑ H_2O , ↓ H^+ , ↓ K)

i. hypernatremia & hypervolemia :

1. Mild HTN. (***never sever***)
2. **No** edema inspite of hypervolemia, it is due to :
   a. renal escape phenomenon.
   b. hypokalemic nephropathy → polyuria.

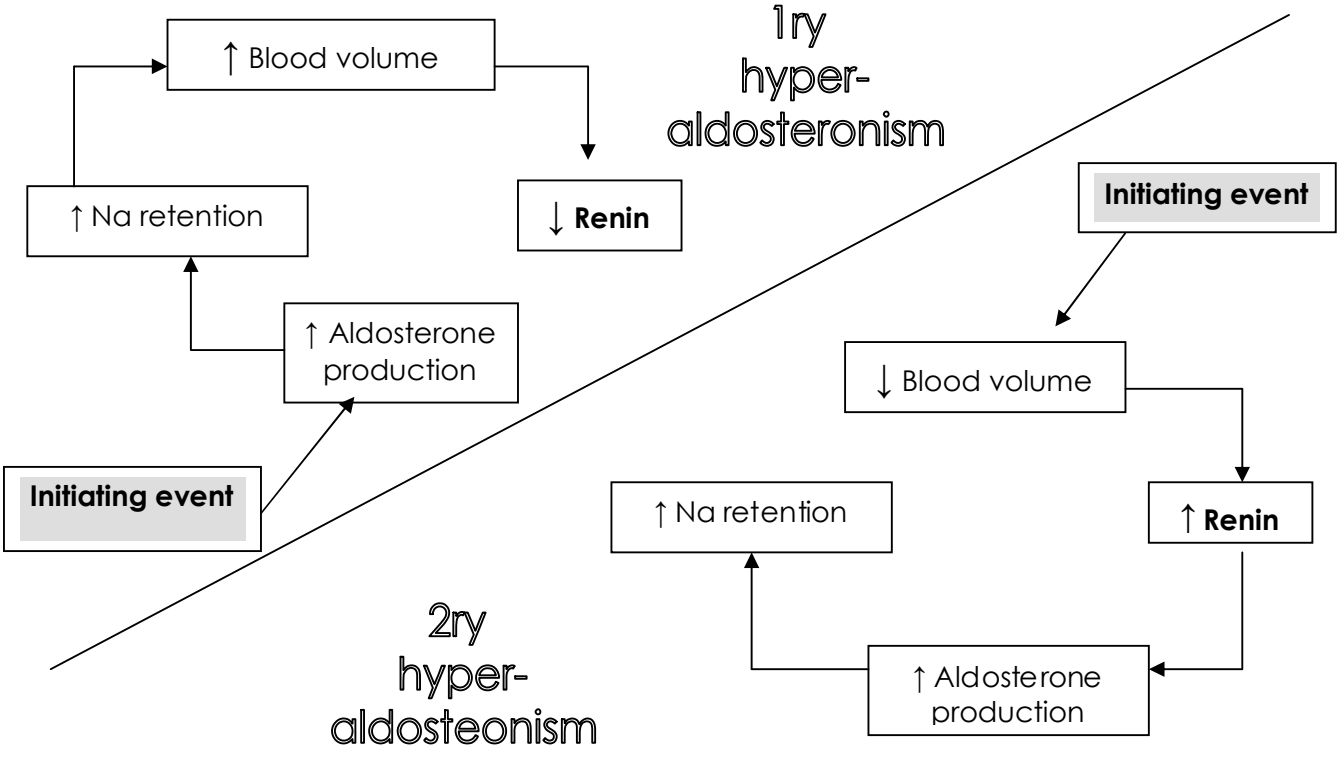
ii. ↓↓ H. (alkalosis) : leading to tetany.

iii. ↓↓ **K. (hypokalemia) :** muscles

1. **skeletal muscles** : weakness, flaccidity up to paralysis.
2. **Smooth muscles (GIT)** : atony, constipation.
3. **Cardiac muscle** : arrhythmia , ECG changes (prominent U wave)
4. **others** : nephropathy , glucose intolerance.

4. Differential diagnosis : form 2ry hyperaldosteronism (*stimulus is extra-adrenal*)

	1ry hyperaldosteronism	2ry hyperaldosteronism
Source	- Adrenal Gland.	- Renal artery stenosis. - Heart failure. - Nephrotic syndrome. - Liver cirrhosis.
Aldosterone	**+++**	**+**
Renin	↓↓	↑↑
HTN	mild.	No HTN except in renal artery stenosis → sever.



5. Investigation :

a. Investigations for the cause : suprarenal gland imaging : US , CT , MRI

b. Assay of the hormone level :

i. In blood :

1. ↑ **aldosterone** in serum (n = 3 -15 ngm%).
2. ↓ **plasma renin** activity (due to -ve feed back)

ii. In urine :

↑ metabolite of the hormone (*tetrahydroaldosterone*)

c. Investigation for the function of aldosterone :

i. Blood :

1. ↓ K. (hypokalemia) [n : 3.5 - 5 mEq/L].
2. ↑ Na. (hypernatremia) [n : 140 mEq/L].
3. alkalosis : ↑ serum HCO3 [n: 22 - 26 mEq/L].

ii. Urine :

1. ↓ Na.
2. ↑ K.
3. ↑ H^+.

6. Treatment :

a. Surgical removal of the tumor.

b. Irradiation.

c. Antagonism :

i. **A**ldosterone antagonist : spironolactone (aldactone 400 mg/d)

ii. **A**CE inhibitors : captopril in 2ry hyperaldosteronism. **MCQ**

d. Symptomatic treatment : excess K & low Na.

Cushing's syndrome

1. Physiology :

a. Hormone : ↑ Cortisol .

b. Gland : Suprarenal gland (*Zona fasiculata*)

c. **Function of the hormone** : 10

i. CHO : hyperglycemia.

ii. Protein : catabolic.

iii. Fat :

1. lipolytic.
2. Redistribution of fat in abnormal sites (face, back of neck, trunk)

iv. Water & electrolyte : (*aldosterone like*)

1. ↑ H_2O & Na.
2. ↓ K & H^+.

v. Stomach : ↑ HCl

vi. Bone : anti-vitamin D action.

vii. Blood : (2 ↑↑ & 3 ↓↓) MCQ

1. ↑ RBCs.
2. ↑ neutrophils.
3. ↓ lymphocytes.
4. ↓ esinophils & basophilis.

viii. Psychosis.

ix. Androgenic action.

x. Anti-inflammatory & anti-allergic.

d. Regulation of the hormone : stimulated by ACTH.

2. Etiology :

a. 1ry (*adrenal Cushing or Cushing syndrome*) : adenoma or adenocarcinoma of zona fasiculata → secreting cortisol [*20 %*].

b. 2ry (*pituitary Cushing or Cushing disease*) : adenoma or hyperplasia of pituitary gland → secreting ACTH [*70 %*].

c. paramalignant syndrome e.g. oat cell carcinoma.

d. Exogenous intake (*Cushinoid picture*).

3. Clinical picture :

a. C / p of the cause : Pituitary tumor , Paraneoplastic syndrome.

b. C / p of the hormone :

i. **CHO** : hyperglycemia & may be secondary DM in 15 %.

ii. **Protein** : catabolic

1. muscle wasting , weakness & fatigue.
2. Capillary fragility : vascular purpura.
3. osteoprosis.
4. thinning of skin, stria rubra , delayed wound healing.

iii. **Fat** : abnormal deposition of fat in :

1. face : moon face with acne.
2. inter-scapular area : buffalo hump.
3. trunkal obesity with thin limbs (samboxa shaped obesity

iv. **Water & electrolyte** : ↑ Na , H_2O & ↓ K , H^+

1. HTN (*due to ↑ Na & ↑ the action of catecholamines*)
2. manifestations of hypokalemia.
3. alkalosis.

v. **Stomach** : peptic ulcer (perforation).

vi. **Bone** : osteomalacia & osteoporosis.

vii. **Blood** : polycythemia (plethoric face) , Recurrent infections

viii. **Psychiatric** : depression & suicidal tendency.

ix. **Androgenic action** :

1. female : amenorrhea, hirsutism.
2. male : ↓ libido , impotence & ↑ body hair.

x. **Skin pigmentation only in 2ry (pituitary) Cushing** due to ↑ ACTH

Causes of death : Cardiovascular disease & infections.

4. Differential diagnosis :

I. DD of the cause : 1ry & 2ry Cushing.

II. Pseudo Cushing :

a. Obese hypertensive diabetic patients.

b. Females taking oral contraceptive pills.

c. chronic alcoholism → impaired liver function → impaired metabolism of corticosteroids.

5. Investigation :

a. Investigations for the cause :

i. Imaging for suprarenal gland : abdomen X-ray , U/S , CT & MRI

ii. Imaging for pituitary gland : Skull CT & MRI .

iii. Imaging for oat cell carcinoma : X-ray , CT chest.

b. Assay of the hormones level :

i. In blood :

1. **cortisone :** ↑ (N : 5 – 20 µgm %)
   - a. early : loss of circadian rhythm (no ↓ of cortisol level by night).
   - b. later : persistent high level .
2. **ACTH :** (N : 60 pg/ml)
   - a. ↑ → pituitary Cushing or Paramalignant syndrome.
   - b. ↓ → adrenal Cushing.

ii. In urine :

urinary free cortisol excretion on 24-hour : ↑, this is the single best biochemical marker of Cushing syndrome. MCQ

c. Investigations of the function of cortisone :

i. Biochemical changes :

- ↑↑ Na.
- ↓↓ K.
- ↑↑ $NaHCO_3$.
- ↑↑ glucose.

ii. Blood picture :

- ↑ RBCs
- ↑ neutrophils.
- ↓ lymphocytes.
- ↓ esinophils.

iii. Urine : ↓ Na , ↑ K , ↑ H^+.

d. Suppression test : (dexamethazone test).

1. Low dose : 0.5 mg / 6h → for 2days.
   i. +ve (↓ cortisol level) → normal.
   ii. –ve (no suppression) → Cushing.
2. High dose : 2 mg / 6h → for 2days.
   i. +ve (↓ cortisol level) → 2ry (*pituitary*) Cushing.
   ii. –ve (no suppression) → 1ry Cushing.

6. Treatment :

a. **Treatment of pituitary Cushing** :

i. Surgical removal or Pituitary irradiation.

ii. Antagonist : Bromocriptine.

Nelson syndrome : big pituitary adenoma with very high ACTH & hyperpigmentation after bilateral adrnalectomy in a case of pituitary Cushing.

b. **Treatment of adrenal Cushing :**

i. Surgery : removal of adenoma followed by cortisol & ACTH.

ii. Adrenocrtical inhibitor : **Metyrapone** (↓ *cortisol synthesis*) *MCQ*

c. **Paramalignant syndrome** : surgical removal of the tumor.

Adrenogenital syndrome

(Congenital adrenal hyperplasia)

1. Physiology :

a. Hormone : Sex hormone (androgen).
b. Gland : Suprarenal gland (zona reticularis).
c. Function of the hormone : Gametogenesis & 2ry sex characters.
d. Regulation of this hormone : ACTH.

2. Etiology :

Enzyme deficiency in the cortical synthetic pathways (21 hydroxylase enzyme) → ↓ cortisol level → ↑ ACTH → act on zona reticularis → ↑ sex hormone secretion

3. C / P : depends on age & sex of the patient.

a. Pre-natal : Female pesudohermaphrotidism :
(small vagina, big fused labia majora simulating scrotum)
b. Post-natal & before puberty :
i. In males : pesudo-precocious puberty (musculinization, deepening of voice, but with small testis & no spermatogenesis
ii. In females : virilism (amenorrhea, musculinization & hirsutism)

N.B. : Hirsutism before menarche is suggestive for congenital adrenal hyperplasia.

c. After puberty : there is virilism in females.

4. Investigation :

a. Investigations for the cause : Imaging for the gland.
b. Assay of the hormones level :
i. In blood : ↑ testosterone , ↑ ACTH.
ii. In urine : ↑ metabolite of testosterone (*17-hydrotestosterone*).

5. Treatment : Cortisone → Suppress ACTH → ↓ Androgens.

Addison's disease

(1ry Chronic adrenal failure)

1. Physiology :

a. Hormone : ↓ **Cortisol** , Aldosterone , Sex hormones.

b. Gland : suprarenal gland (3 zones).

c. Function of the hormones : *see before*.

d. Regulation of the hormone : *see before*.

2. Etiology :

a. **Autoimmune** → 80%

b. **Tuberculosis** → 15%

c. Surgery. d. Irradiation.

e. Sarcoidosis & Heamochromatosis. ♫♫

3. C / P :

a. C / p of the cause : TB , Surgery.

b. C / p of the hormone :

i. **Hypoglycemia** : (due to ↓ cortisone)

1. drowsiness, lack of concentration, hunger pain, coma.
2. There may be absence of the usual warning signs due to lack of adrenaline (notice that ↓ cortisone →↓ action of catecholamine)

ii. **Hypotension** : (due to ↓ cortisone & aldosterone)

1. ↓ Cortisol & aldosterone → ↓ Na → Hypovolemia & decreased response of the blood vessels to the action of catecholamines → hypotension.
2. postural hypotension is common due to ↓ action of catecholamines.

iii. **Hyper-pigmentation** : (due to high level of ACTH)

1. ↑↑ACTH → direct action on melanocytes.
2. It is <u>not present</u> in secondary adrenal failure.
3. sites :
   a. sun exposed areas : face & neck.
   b. friction areas : elbow.
   c. pigmented areas : areola.
   d. scars .
   e. mucous membrane : mouth & tongue.

iv. **GIT manifestations :**

1. diarrhea → 85%.
2. constipation → 15%.
3. anorexia, nausea, vomiting.
4. **abdominal pain** : due to↓ Na , tender renal angle due to TB.

v. **Asthenia** : marked muscle weakness & loss of weight due to :

1. ↓ aldosterone → hyperkalemia & hyponatremia.
2. ↓ cortisol → hypoglycemia.
3. ↓ androgens → -ve nitrogen balance.

vi. **Others**

1. polyuria : due to Na diuresis.
2. neuropathy.
3. infertility in males & amenorrhea in females.
4. Associated autoimmune diseases.

vii. **Addisonian crisis** : *see later*

4. Differential diagnosis :

a. 2ry adrenal insufficiency :

- Hypopituitarism → ↓ ACTH → ↓ cortisone & ↓ androgen with no ↓ aldosterone.
- In 2ry adrenal failure there are :
  - No skin pigmentation. (due to ↓ ACTH)
  - Minimal hypotension (due to normal aldosterone).
  - Manifestations of panhypopituitarism.

b. Skin pigmentation :

- Endocrinal diseases : 1ry Addison , 2ry Cushing , DM , thyrotoxicosis.
- Chronic renal failure.
- Malignancy. - Pregnancy. ♫♫
- Heamochromatosis. - 1ry biliary cirrhosis. ♫♫
- skin diseases.

5. Investigation :

a. **Investigations for the cause** :

i. Imaging for suprarenal gland : Abdominal U/S , CT, MRI.

ii. Adrenal antibodies : in autoimmune cases.

b. **Assay of the hormones level** :

1. Cortisol level : low [n. 5 -20 µgm%]
2. ACTH level : ↑ in 1ry adrenal failure , ↓ in 2ry adrenal failure

c. **Investigations of the function of i hormone** :

i. Biochemical changes :

1. ↓ (Na & glucose).
2. ↑ (K , Ca & H^+).

ii. Blood picture :

1. ↓ (RBCs & neutrophils)
2. ↑ (lymphocytes & esinophils).

d. **Stimulatory test :** (***ACTH stimulation test***)

Synacthen (*synthetic ACTH*) is given IM or IV & plasma cortisol levels are estimated at 0 , 30 , 60 minutes.

- +ve (↑ cortisol level) → 2ry adrenal failure.
- –ve (no stimulation) → 1ry Adrenal failure.

6. Treatment :

a. Treatment of the cause e.g. TB.

b. Diet : ↑ (Na , CHO & protein).

c. Replacement therapy :

i. Oral cortisone (predinsolone : 7.5 mg/d).

ii. Flurocortisone : 0.1 mg/d to replace aldosterone, especially in severe hypotension.

Addisonian crisis

(Acute adrenal failure)

Etiology :

i. Acute on top of chronic :

1. Addison's disease subjected to : surgery , infection, bleeding.
2. Panhypopituitarism : if treatment is initiated with thyroxin without cortisol.

ii. Acute from the start :

1. surgery : bilateral adrenalectomy.
2. sudden withdrawal of chronic cortisone therapy.
3. meningococcal septicemia (Waterhouse-Freidrichon's syndrome)
4. massive thrombosis of adrenal vein.

C / P :

a. **C / p of the cause** : Surgery, Infection.

b. **C / p of the hormone** :

1. *Sever* hypoglycemia → coma.
2. *Sever* hypotension → shock.
3. *Sever* asthenia → confusion.
4. *Sever* skin pigmentation → desquamation.
5. *Sever* diarrhea → dehydration & acute abdomen.

Investigation : As Addison's disease.

Acute adrenal failure should be suspected in any patient in the ICU who develops hypotension of unclear etiology or has refractory hypotension (*hypotension not corrected by saline & vasopressors*)

Treatment : *medical emergency*

i. **IV fluids :**

- 1 - 2 L of normal saline (*0.9 % NaCl*).
- 1 - 2 L of 10% glucose.

ii. **Cortisone is started** *immediately* as follow :

- Hydrocortisone , 50 - 100 mg /6 h **IV** until the patient is clinically stable then shift to oral cortisone.
- Dexamethasone (*Decadron*) can be given before or during the ACTH stimulation test. *It will not interfere with plasma cortisol assay*.

iii. **Treatment of the precipitating factors :** e.g. infection or DIC.

Pheochromocytoma

(Hyperfunction of adrenal medulla)

- It's the commonest tumor arising from the adrenal medulla.
- **Rule of 10** :
  - **10 %** familial.
  - **10 %** bilateral.
  - **10 %** malignant.
  - **10 %** extra-adrenal (*in the sympathetic chain*).

C / P :

a. Paroxysmal hypertension.
b. Paroxysmal headache.
c. Paroxysmal sweating.
d. Paroxysmal tachycardia (palpitation)
e. Anxiety & psychiatric disturbance.

Investigation :

a. Urinary ↑↑ VMA (*Valenyle Mandelic Acid*) : ↑
b. Urinary catecholamine : ↑
c. Plasma catecholamine : ↑
d. CT scan , MRI for abdomen.
e. Radioisotope scanning : scanning with **M**eta **I**odo **B**enzyl **G**uanidine (**MIBG**) produces specific uptake in sites of sympathetic activity.

Treatment :

a. Surgery is the treatment of choice.
b. Medical : combined α & β blockers.

☠ If you start with β blocker → unopposed α action → Hypertensive crisis.

Steroid preparations

Uses :

1. **Replacement therapy** :
    a. Addison's disease.
    b. Congenital adrenal hyperplasia.

2. **Supplementary therapy in non endocrine diseases :**
    a. Anti-inflammatory & anti-allergic :
        i. CNS :
            1. cerebral edema with neoplasm.
            2. ↑ ICT.
        ii. CVS :
            1. rheumatic fever.
            2. Post infarction syndrome (*Dressler's syndrome*)
            3. hemolytic anemia.
            4. ITP.
        iii. GIT :
            1. ulcerative colitis & Crohn's disease.
            2. chronic hepatitis.
        iv. Respiratory :
            1. bronchial asthma .
            2. COPD.
            3. sacroidosis.
        v. Renal : certain types of GN.
        vi. Collagen disease : SLE , polymyositis ,PAN , Rh.arthritis.
        vii. Allergic disease : anaphylaxis.
        viii. Inflammatory conditions :
            1. eye → conjunctivitis.
            2. skin → eczema.
    b. Anti-stress & anti-shock.

3. **Suppression therapy :**
    a. Tissue transplantation.
    b. Lymphoma & leukemia.

Side effects & contraindications :

	Side effect	*Contraindication*
1. From prolonged treatment		
a-Metabolism :		
▪ **CHO**	- Hyperglycemia.	- D.M.
▪ **Fat**	- Moon face. - Buffalo hump.	- Cushing syndrome.
▪ **Protein**	- Osteoporosis. - muscle weakness.	- Myopathy. - Wasting.
▪ **Electrolytes**	- Na & water retention. - Hypokalemia. - Hypocalcaemia.	- Hypertension. - Hypokalemia. - Rickets & osteoporosis.
b-Systems :		
▪ **General**	- Delay healing of wound.	- Uncontrolled infection.
▪ **Eye**	- Cataract. - Glaucoma.	- Cataract. - Glaucoma.
▪ **CNS**	- Nervousness. - Insomnia. - Psychosis.	- Psychosis.
▪ **CVS**	- HTN. - HF. - Thrombosis.	- HTN. - HF.
▪ **Respiratory**	- Chest infections.	- T.B.
▪ **GIT**	- ↑ Gastric acidity.	- Peptic ulcer.
▪ **Genital**	- Teratogenecity. - Menstrual disturbance. - Hirsutism.	- Pregnancy.
2. From sudden withdrawal of steroids		
	- Addisonian crisis.	- Sudden withdrawal.

Diabetes mellitus

Definition:

It's a **clinical syndrome** in which there is an error of CHO metabolism ; due to insulin deficiency, resistance or both, ending in : chronic hyperglycemia ± glucosuria, vasculopathy & neuropathy.

Etiology : (1ry → 95% & 2ry → 5%)

I. **Primary** : (includes 3 types :)

a. Type 1 : previously called **I**nsulin-**D**ependant **DM** (IDDM) or juvenile-onset DM.

b. Type 2: previously called **n**on **i**nsulin-**d**ependant **DM** (NIDDM) or adult-onset DM

c. MODY : **m**ature **o**nset **d**iabetes in **y**oung patient.

- intermediate between type 1 & type 2.
- Treatment : oral anti-diabetic drugs.

> The old classification of insulin dependant & non-insulin dependant DM is misleading because many patient type 2 DM eventually require insulin for control hyperglycemia.

II. **Secondary D.M.** :

a. Pancreatic causes e.g. Chronic pancreatitis .

b. Endocrinal : Cushing , Acromegaly , Thyrotoxicosis.

c. Drugs : Cortisone, Thiazide , Contraceptive pills.

d. Others : Gestational diabetes , DIDMOAD syndrome.

Pathogenesis :

Type 1 : 10%.

- An **autoimmune** destruction of the pancreatic β-cells leads to absolute insulin deficiency.
- Genetic factor play an important role (*the combination of HLA **DR3** & **DR4** makes a person more likely to develop type 1 DM*)

- viral infection may play a role.
  - without insulin, these patients are prone to develop ketoacidosis.
  - Although typically diagnosed before age 30, it can present at any age due to variability in rate of β-cell destruction.

Type 2 : 85%

- It's characterized by peripheral insulin resistance, so hyperglycemia develops despite above average level of insulin.
- In addition, it may be due to abnormal structure of insulin or due to anti-insulin hormones e.g. glucagons.
- Factors that may play a role in pathogenesis include : genetic predisposition & obesity.

	Type 1	Type 2
▪ **Incidence** :	10 %	85%
▪ **Pathogenesis** :	Insulin deficiency due to damage of β-cells.	Insulin resistance.
▪ **Insulin level** :	↓↓	Normal or even ↑↑
▪ **Age of onset** :	Younger (usually < 30y).	Older (usually > 30y).
▪ **Body weight** :	Thin.	Obese (usually 80 %).
▪ **Hereditary** :	- 30% in identical twins - usually no family history.	- Near 100% - strong family history.
▪ **C / P** :		
- **Severity** :	Sever.	Mild or moderate.
- **Ketoacidosis** :	Common.	Rare, need ppt factors.
- **Complication** :	More common.	Less common.
▪ **Treatment** :		
- **Oral hypoglycemic**	Ineffective.	Effective.
- **Insulin** :	Necessary (*essential for life*)	Usually not required

Stages of DM :

I. **Pre diabetes** : (*impaired glucose tolerance*)

a. It refers to a group of people who have glucose values too high to be considered normal but not fit the criteria for the diagnosis of DM (**fasting blood glucose > 110 & < 126 mg%**)

b. It's an intermediate category between normal & DM.

c. There is risk factor for future diabetes & CVS diseases.

d. This group includes :

i. +ve family history. ii. obesity.

iii. ♀ with bad obstetric history → macrosomia.

iv. renal glucosuria.

II. **Latent diabetes** :

Diabetes appears only on exposure to stress & disappears after removal of stress e.g. pregnancy.

III. **Chemical diabetes** : Raised blood glucose with no symptoms.

IV. **Clinical diabetes** :

a. ***Uncomplicated*** : Classic triad of symptoms : 3 **p**

- **p**olyuria : due to osmotic diuresis induced by sugar.
- **p**olydepsia : due to loss of fluid.
- **p**olyphagia with weight loss : ↓ insulin → no glucose can enter satiety center → ↑↑ of satiety center. While loss of weight is caused by fluid depletion , fat & muscle breakdown.

b. ***Complicated*** : May be the 1st presentation. *see later*

Investigations of DM :

I. Blood :

1. Blood sugar tests :

i. Fasting blood glucose : (***no caloric intake for at least 8 hours***)

- 70 - 110 mg % → normal.
- > 126 mg % → DM.
- 110 - 126 mg % → impaired glucose tolerance.

ii. 2 h. post-prandial : (***after ingestion of 75 gm glucose***).

- < 140 mg % → normal.
- > 200 mg % → DM.
- 140 - 200 mg % → impaired glucose tolerance.

i. Random (*casual*) glucose level : it means glucose level during any time of day regardless to last meal.

2. Oral glucose tolerance test : (OGTT)

i. Patient should be fasting over night.
ii. Fasting blood sugar is done.
iii. The patient is fed 75 gm glucose orally.
iv. Take blood & urine samples every 1/2 h. for 2 h.
v. Normal curve : *3 criteria*
   1) Fasting : 70-110 mg %
   2) Reach maximal point in 1h. but still under 180 mg %
   3) Return to normal within 2 h.

3. Cortisone glucose tolerance test :

i. Dexamethazone 3 mg is given before OGTT.
ii. It will induce hyperglycemia in latent & pre diabetes.

II. Urine :

1. Glucosuria : occurs when glucose serum level exceeds 180 mg % (*renal threshold*); but it's not a good indicator for DM diagnosis.
2. Ketonuria : for diagnosis of diabetic ketoacidosis.

III. Monitoring of treatment :

1. Plasma glucose monitoring.
2. Glycosylated hemoglobin (**HBA1c**)

i. Normally it's less than 7 % of total HB.
ii. > 12% → poor glycemic control in the past 3 months.

IV. Investigations for complication :

1. Plasma lipids.
2. Urine analysis.
3. ECG.
4. Chest X-ray .

V. Investigations for the cause : If 2ry diabetes is suspected (< 5 %)

New WHO diagnostic criteria : ***2 of these 3 criteria*** **:**

1- Fasting plasma glucose > 126 mg %.

2- Random plasma glucose > 200 mg %.

3- Classic triad of diabetic symptoms (3p).

Pathogenesis of diabetic complications :

1. **Glycosylation :**

   This may lead to thickness of basement membrane of capillaries with narrowing of their lumen → leading to vasculopathy.

2. **Sorbitol pathway :**

   Glucose is reduced to sorbitol by aldose reductase → ⇩ of ATPase activity → leading to neuropathy & nephropathy.

Complications of DM

Cutaneous :

1. Infection : carbuncles & recurrent abscesses.
2. Pruritis : pruritis vulvae.
3. Delayed healing of the wounds.
4. Xanthelasma ; due to hyperlipidemia.
5. **Necrobiosis diabeticorum** :
   a) Red **p**ainless **p**apules with yellow center.
   b) usually over the anterior surface of the legs.
   c) due to cutaneous blood vessels occlusion.
6. Cutaneous features of diabetic foot.
7. Acanthosis nigricans : black patches due to insulin spillover into the skin in type 2 DM. ***MCQ***
8. Lipodystrophy : at the sites of insulin injection.

Cardiovascular :

1. **Microangiopathy** :
   a) Diabetic retinopathy → retina.
   b) Diabetic nephropathy → glomeruli.
   c) Diabetic neuropathy → vasa nervosa.
2. **Macroangiopathy** :
   a) cerebral : thrombosis & ischemia.
   b) coronary : angina & MI ,may be painless due to neuropathy
   c) peripheral : gangrene & intermittent cludication.
   d) renal : reno-vascular hypertension.
3. **Cardiomyopathy** : due to microangiopathy.
4. **Blood pressure** :
   a) systemic hypertension.
   b) postural hypotension due to autonomic neuropathy.

Causes of HTN in diabetic patient :

1- Diabetic nephropathy.
2- Endothelial dysfunction.
3- Insulin → retention of Na.
4- 2ry diabetes : Cushing & acromegaly.
5- Type 2 DM may be a part of metabolic syndrome X which consists of :
(DM , hypertension , Hyperlipidemia, obesity).

Chest :

1. Recurrent chest infection e.g. T.B. **(*T.B. follows DM as its shadow*)**.
2. Kussmaul respiration (*air hunger*) & acetone smell in DKA.

Gastrointestinal :

*Diabetics **never** have normal bowel habits*

1. **Mouth** : gingivitis , loosening of teeth.
2. **Stomach** :
   - o gastroparesis .
   - o Nausea , vomiting & abdominal pain in DKA.
3. **Intestine** :
   - o Diarrhea : due to sympathetic neuropathy , vasculopathy & GIT infections.
   - o Constipation : due to vagal neuropathy.
4. **Liver** : fatty liver.
5. **Gall bladder** : chronic cholecystitis , gall stones.

Genital :

1. In ♂ : impotence (*psychological, neuropathy, vasculopathy*)
2. In ♀ : infections & pruritis vulvae.
3. **Effects of DM on pregnancy** :
   - On mother :
     i. Eclampsia.
     ii. post Partum hemorrhage.
     iii. puerperal sepsis.
   - On fetus :
     iv. High birth weight.
     v. Hypoglycemic baby.
     vi. Congenital anomalies.
4. **Effects of pregnancy on DM :**
   i. ↑ needs for insulin due to ↑ anti-insulin : estrogen.
   ii. ↓ renal threshold for glucose.
   iii. ↑ incidence of complications.

Eye :

1. **Lids** : infection (chalazion , conjunctivitis) , Xanthelasma.
2. **Iris** : New vessels formation in iris (rubeosis iridis)
3. **Lens** :
   - Senile cataract (*occur at an earlier age*)
   - Repeated error of refraction secondary to osmotic lens changes with fluctuating glucose level :
     - Hyperglycemia leads to myopia.
     - Hypoglycemia leads to hypermetropia.
4. **Nerves** :Optic neuritis , Cranial nerve palsy (3, 4 & 6 nerves).

5. ***Diabetic retinopathy*** :

a. It's the most characteristic form of diabetic eye diseases.
b. It is related to the duration & control of the disease.
c. It eventually occurs in nearly <u>all</u> patients of type 1 DM 10 years after diagnosis. It is present in 10% of type 2 DM at diagnosis, 50% after 10 years and 80 % after 20 years.
d. It is usually accompanied by nephropathy & neuropathy.
e. Detected by *fluorescin angiography*.
f. There are 2 important types :

- Non proliferative (*background retinopathy*) :

- ✓ Characterized by ↑ capillary permeability, Microaneurysms , hemorrhage , exudates .
- ✓ During this stage of diabetic retinopathy, no local treatment required , *except in a case of* ***diabetic maculopathy***, just good control of diabetes and of any coexisting hypertension and stopping smoking ,

- Proliferative :

Characterized by neovascularization, retinal detachment. this type must be treated as early as possible by laser *photocoagulation*.

💣 *without treatment 50% of proliferative patients become blind within 5 – 10 years.*

- *Proliferative retinopathy : more common in type 1 DM.*
- *Diabetic maculopathy : more common in type 2 DM.*

Renal :

1. **Interstitial injury :**

   - Pyelonephritis : ▪ Fever ▪ Pain. ▪ Dysuria. 👌

   - Acute necrotizing papillitis : fever , pain , dysuria and hematuria.

2. **Diabetic nephropathy :** ***(Diabetic glomerulosclerosis)***

Definition :

clinical syndrome characterized by ↑ in urine albumin excretion ,↑ BP up to end stage renal failure with progressive rise in CV risk.

Incidence :

- long standing DM (30% type1 , 20 % type2) .
- Genetic factor may play a role.

Pathogenesis : **Glomerular sclerosis** :

i. Early Thickening of basement membrane of glomeruli & mesangial expansion .

ii. Hyalinization of afferent & efferent arterioles.

Glomerular hyperfilteration ⇨ proteinuria ⇨ end stage renal disease.

DM affects efferent more than afferent arterioles . So ; there is more narrowing in efferent than in afferent, this ↑↑ intra-glomerular pressure ⇨ this will allow plasma proteins to escape into the urine ⇨ Some of these proteins will be taken up by the proximal tubular cells, which can initiate an inflammatory response that contributes to interstitial scarring eventually leading to fibrosis.

Types :

i. Diffuse : 80 %.

ii. Nodular : 20 % (*Kimmelestiel-Wilson's syndrome*).

Clinical picture :

i. Long standing DM especially poorly controlled diabetes after about 10-20 years .

ii. Proteinurea : ***the early clinical sign of diabetic nephropathy***

1. micro-albuminuria : 30-300 mg/day It is reversible by **ACEIs** .
2. macro-proteinuria : > 300 mg/day
3. heavy proteinurea (nephrotic syndrome)

Nearly 100% with gross proteinuria will progress to End Stage CRF in 5 – 15 y ☹

iii. Lately, progressive loss of renal function (**CRF**) .

iv. Hypertension, diabetic retinopathy& neuropathy are usually present.

Stages of diabetic nephropathy : *for postgraduates*

A) Incipient nephropathy :

- **Stage I :** nephromegally , ↑ GFR.
- **Stage II :** stage I + microalbuminuria on exercise.
- **Stage III :** as stage 2 but persistent microalbuminuria > 30 mg/d. This stage may remain silent for up to 10 – 15 years.

B) Overt nephropathy :

- **Stage IV :**
  - ✓ Macro proteinuria > 300 mg/d . (rarely the proteinuria exceed 5 gm /d)
  - ✓ ↓ GFR.
  - ✓ Hypertension is common.
- **Stage V :** End stage CRF.

Investigation :

1- Urinalysis : **Screening of microalbuminuria** is a mandatory .

It should be performed in type 1 patients who have had diabetes > 5 years and all type 2 diabetic patients starting at diagnosis (In type 2 DM , microalbuminuria can be present at the time of diagnosis).

2- Blood : urea & creatinine.

3- U/S : normal or large kidney. (not shrunken as usual CRF) ***MCQ***

4- Biopsy : may be done if there is any doubt in the diagnosis. It is not always necessary if the case is straightforward, with a documented progression of proteinuria over time and presence of diabetic retinopathy.

Treatment :

1- Diabetic control can reverse the microalbuminuria.

2- Control of hypertension is a mandatory by **ACEIs & ARBs** which decrease the albuminuria even in normotensive patients.

3- Treatment of CRF : **3D + T** *see nephrology*

- **D**iet : low protein diet
- **D**rugs : symptomatic treatment.
- **D**ialysis.
- **T**ransplant : treatment of choice in young patients.

Diabetic foot :

Definition : Trophic changes in foot of diabetic patients (ulcers, falling of hair & gangrene).

Etiology : vasculopathy, neuropathy & infection combine to produce tissue necrosis.

Treatment :

a) Control of diabetes.
b) Careful foot cleaning & careful nail cutting.
c) For infection : strong antibiotic & drainage of pus.
d) For ischemia : revascularization & amputation in gangrene.

Diabetic infections :

1. skin : staph & candida .
2. urinary tract : pyelonephritis & perinephric abscess.
3. Chest : T.B. & pneumonia.
4. Genital : pruritis vulva.
5. GB : cholecystitis.

Neurological :

I. Diabetic macroangiopathy

II. Diabetic neuropathy.

III. Diabetic comas.

I. **Diabetic macroangiopathy :** (*due to atherosclerosis*)

a. Cerebral hemorrhage.

b. Cerebral thrombosis.

II. **Diabetic neuropathy :**

Pathogenesis : *unknown* but there are 4 important theories :

1. Hypovitaminosis : polyuria washes water soluble B complex.
2. Microangiopathy of vasa nervosa.
3. Metabolic ketosis : toxic effect of keton bodies.
4. **Transformation of glucose to sorbitol by aldose reductase enzyme.**

C/P : (may precede the discovery of DM)

1. mononeuropathy or mononeuropathy multiplex, affecting :
   a. Peripheral nerves : femoral , ulnar & median nerves.
   b. Cranial nerves : 3 , 4 , 6 . *MCQ*

2. polyneuropathy :
    a. Sensory affection is more than motor affection.
    b. Superficial sensation : Symmetrical parasthesia especially in LL followed by stock & glove hyposthesia.
    c. deep sensations : nocturnal calf spasm is common.
    d. Motor weakness is late.

3. Autonomic neuropathy :

- CVS :

- **P**ostural hypotension.
- **P**ainless myocardial infarction.
- **P**ersistent tachycardia .

- GIT :

- Gastroparesis : delayed gastric empting.
- Diarrhea : severe, nocturnal & alternating with constipation.

- Genito-urinary :

- ✓ **I**mpotence.
- ✓ **I**ncontinence.

- Skin :

- Generalized sweating.
- Edema of the feet due to loss of the vasomotor tone.
- Trophic ulcers.

Treatment :

- Strict control of DM : diet, oral hypoglycemic or insulin.
- Reassurance may be all that needed.
- Physiotherapy if motor weakness is present.
- Drugs : *Low benefit*

a. Analgesics of neurotic pain : carbamazepine (*Tegretol*)

b. Vit. B complex (*Tri B*) & ATP (*adenoplex*).

c. Aldose reductase inhibitors : sorbinil.

d. Cerebrolysin. (*nerve growth factor*)

III. Diabetic comas :

1. Hypoglycemic coma. (insulin reaction)
2. Diabetic ketoacidosis. (DKA)
3. Hyperglycemic hyperosmolar non ketotic coma.
4. Diabetic lactic acidosis.
5. Other causes of coma : uremic, hepatic, ...

Hypoglycemic coma

a. **Etiology** :

- Missed meal or severe exercise after insulin or oral hypoglycemic drugs.
- Over dose of insulin or decreased elimination of insulin as in cases of renal failure.

b. **C/P** : severity of symptoms can vary with the individual.

i. **Adrenergic symptoms** : (*warning signs*)

due to ↑ catecholamines when blood glucose < 50 mg %

1- **T**achycardia (palpitation).

2- **S**weating.

3- **T**remors.

4- **A**nxiety.

5- **H**unger pain.

ii. CNS symptoms :

due to cerebral dysfunction when blood glucose < 30 mg %

1- Headache.

2- Blurring of vision.

3- Lack of concentration.

4- Convulsion may occur.

5- Coma.

Masked symptoms of hypoglycemia may occur in the following conditions : (*not associated with adrenergic symptoms*)

- During night.
- β-blockers.
- Old age.
- Recurrent hypoglycemia.

c. **Investigation** :

Low blood glucose < 50 mg % in male & 45 % in female.

d. **Differential diagnosis** :

- From diabetic ketoacidosis : *see later.*
- From other causes of hypoglycemia : *see later.*

e. **Treatment** : *Recovery is very rapid except in irreversible brain damage*

i. If patient is conscious : oral glucose in the form of candy.

ii. If there is coma : IV glucose 50 gm 50 % .

iii. Hypoglycemia due to oral hypoglycemic drugs (*sulphonylurea*) : may persist for long time (days) so glucose has to be infused for long time.

Diabetic ketoacidosis " DKA "

a. **Definition** :

DKA is an extremely serious metabolic complication of DM due to **sever** insulin deficiency, it's characterized by triad of : 👌

- Acidosis. - Ketosis. - Hyperglycemia (usually >250 mg %).

NB : *There is no relation between the severity of hyperglycemia & the severity of ketoacidosis.*

b. **Etiology** : ketONE bodies are seen in type ONE DM ☺

- Occurs mainly in type 1 DM, due to sever insulin deficiency e.g :
  - Previously un diagnosed DM
  - Missed insulin (neglected treatment).
- Precipitating factors :
  - Infections (*lead to increased insulin requirements*).
  - Infarction (I mean myocardial infarction).
  - Intoxication (Alcohol).

In type 1 DM : DKA occurs with or without Precipitating factors.
In type 2 DM : DKA occurs with Precipitating factors only.

c. **Pathogenesis & C/P** : sever insulin deficiency leads to : 🖐

i. **Glucose can't enter the cells** → hyperglycemia > 250 mg %.

ii. **Fat :** ↑↑ **lipolysis** to produce energy → ↑ production of ketone bodies (β-hydroxy buteric acid, acetoacetic acid & acetone) → ketoacidosis (PH < 7.3)

iii. **Effects of ketoacidosis** : gradual onset of : 🖐 X 2

1- Muscles :
   a. generalized weakness.
   b. muscle pain.

2- Kidney : ketonuria together with glucosuria lead to sever
   a. polyuria.
   b. dehydration.

3- GIT :
   a. Anorexia , nausea & vomiting.
   b. **abdominal pain**.
4- Respiration :
   a. Kussmaul respiration (deep rapid)
   b. acetone odour of breath.
5- CVS :
   a. depressed contractility & low blood pressure.
   b. rapid weak pulse.

iv. **Hyperkalemia** due to Shift of K outside cells in absence of insulin.
v. **Coma** due to combined effect of :
   1. ketone bodies.
   2. dehydration.
   3. electrolyte disturbance.

d. Investigations :

i. **Blood examination** :
   - ↑ glucose > 250 mg %.
   - ↑ ketone bodies.
   - Acidosis (PH < 7.3) with high anion gap.
   - ↑ FFA.
   - Electrolytes : ↑↑ **K** & ↓↓ Na .

ii. **Urine examination** : Polyuria , glucosuria & ketonuria.

e. Treatment :

i. Insulin :

- short acting soluble insulin.
- Regimen : *2 methods*
  a. IV insulin infusion : 5 – 10 u/ h infusion . when blood glucose < 250 mg /dl → reduce insulin to 2 – 4 u/h
  b. Repeated IM : 20 U at the start then 6 U/ h
- The goal is to decrease the blood glucose by 75 mg % / hour.

ii. Fluid therapy :

- 4 – 8 L is usually required.
- 1 L / hour for the first 2 hours followed by $^1/_2$ L / hour until the deficit is replaced.
- At first normal saline is given, then change to dextrose saline when blood glucose < 250 mg/dl.

iii. **K therapy** :

The serum K falls during insulin therapy (*intracellular shift*), and this fall may be dramatic. so add (20 – 40 mEq) to each 1L saline.

iv. **Na bicarbonate :** in sever acidosis [PH < 7.1]

v. **Treatment of precipitating factors** e.g. infection : antibiotics.

	Hypoglycemic coma	**DKA**
▪ ***History :***	- Missed meal.	- Missed insulin.
▪ ***Onset :***	- acute.	- gradual.
▪ ***Pulse :***	- Strong .	- Weak & rapid.
▪ ***Bl.P. :***	- ↑	- ↓
▪ ***Skin :***	- Sweaty.	- **d**ry.
▪ ***Pupils :***	- dilated.	- normal.
▪ ***Respiration:***	- normal.	- Rapid , deep.
▪ ***Urine :***	- normal.	- +ve sugar & acetone.
▪ ***Coma :***	- Irritable.	- not irritable.
▪ ***IV glucose :***	- rapid recovery.	- no effect.

Hyperglycemic hyperosmolar non ketotic coma (HHNK)

- There is low insulin level which is enough to prevent ketosis , but not enough to inhibit hyperglycemia, so there is hyperglycemia without ketosis.
- It occurs in old type 2 DM.
- Patients typically having sever hyperglycemia (> 600 mg/dl), sever dehydration . plasma osmolarity > 340 mOsm/L (N : 290) is the landmark of this condition.
- **Clinical picture** :
    - Severe hyperglycemia : polyuria , polydepsia.
    - Severe dehydration ⇨ renal failure & thrombotic complications.
    - severe hyperosmolarity ⇨ CNS symptoms (convulsions , coma).
- **Treatment** : The same as DKA but
    - Aggressive fluid replacement. (***the most important measure***)
    - Low rate of Insulin infusion (3 U/h).
    - S.C. heparin to prevent thrombotic complications.
    - Na bicarbonate is not given.

Lactic acidosis

- It occurs in diabetics using high dose of biguanides e.g. *metformin*
- Biguanides ⇨ tissue hypoxia ⇨ anaerobic glycolysis ⇨ accumulation of lactic acid.
- C/P :
    a. Rapid deep respiration (Kussmaull respiration).
    b. Confusion , coma.
- Treatment : NaHCO3

DIAGNOSTIC CRITERIA OF DIABETIC COMAS

DKA	HHNK	Lacctic acidosis
✓ Hyperglycemia > 250 mg/dL. ✓ Acidosis with blood pH < 7.3. ✓ Serum bicarbonate < 15 mEq/L. ✓ Serum positive for ketones.	• Hyperglycemia > 600 mg/dL. • Serum osmolality > 310 mosm/kg. • No acidosis; blood pH above 7.3. • Serum bicarbonate > 15 mEq/L. • Normal anion gap (< 14 mEq/L).	o Severe acidosis with hyperventilation. o Blood pH below 7.30 o Serum bicarbonate < 15 mEq/L. o Anion gap > 15 mEq/L (*high anion gap*) o Absent serum ketones. Serum lactate > 5 mmol/L

- ***Acute diabetic complications : diabetic coma + infections.***
- ***Micro-vascular complications : diabetic triopathy.***
- ***Hyperglycemic coma : DKA , HHNK.***

Treatment of DM :

I. General measures.

II. Diet.

III. Oral hypoglycemic.

IV. Insulin.

V. Treatment of complications.

I. General measures :

a. Reassurance.

b. Education about nutrition & lifestyle modifications.

c. Exercise.

II. Diet :

a. It's an important item in control of D.M.

b. Diet alone can control mild cases of type II D.M.

c. **Total calories/day :** *depending on weight & physical activity*

i. Mild activity → 1500 cal/d.

ii. Moderate activity → 2500 cal/d.

iii. Severe activity & pregnancy → 3500 cal/d.

d. Food components :

i. CHO : 50% of calories . avoid simple sugars.

ii. fat : 30% of calories . avoid saturated fat.

iii. protein : 20% of calories.

iv. vitamins : B-complex & vit. A

v. ↑↑ fibers : ↑ satiety.

e. Number of meals :

3 main meals + 2 snacks in between, to avoid hyperglycemia or hypoglycemia .

III. Oral hypoglycemic

a. Sulphonylureas :

- mechanism of action :

1. ↑↑ insulin secretion from pancreas.
2. ↑↑ peripheral action of insulin.
3. ↓↓ hepatic production of glucose.

- **preparations :**

Drug	Trade name	Dose (mg/d)	Duration of action
▪ **Old generation :**			
- Cholropropamide	*Pamidine*	100 - 500	long acting
- Tolbutamide	*Diamol*	500 - 3000	short
▪ **New generation :**			
- Glibenclamide	*Doanil.*	2.5 - 15	long acting
- Glimepiride	***Amaryl.***	1 - 6	long acting
- Gliclazide	***Diamicron.***	80 - 480	intermediate
- Glipizide	*Minidiab*	2.5 - 30	short

- **Indication :**

type 2 DM not controlled by diet alone especially in non obese patients.

- **Side effect :**
  - **A**llergy.
  - **A**plastic anemia.
  - **H**ypoglycemia.
  - **H**epatitis.
  - **H**yponatremia due to increased ADH by cholropropamide.

b. Biguonides :

- **Mechanism of action :**
  1. ↑ anaerobic glycolysis.
  2. ↓↓ intestinal glucose absorption. 3. ↓↓ appetite.
- **preparations :** Metformin *(Cidophage)* 500 - 850 mg t.d.s.
- **Indications :**
  1. type 2 DM not controlled by diet alone esp. in obese patients.
  2. combined with suphonylurea or insulin to achieve control.
- **Side effects :**
  - GIT irritation.
  - lactic acidosis.

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  - GIT irritation.
  - lactic acidosis.

b. Recent drugs :

i. **Alpha Glucosidase inhibitors** : Acarbose *(Glucobay)* 50 mg t.d.s.
prevent breakdown of CHO in intestine ⇨ ↓ glucose absorption.

ii. **Pioglitazone** (*Diabetin*) : ↑ tissue sensitivity to insulin (*insulin sensitizer*)

A physician without differential diagnosis is like a soldier without his gun, like a clown without his fun.

Dr/Alsayed Dawoud
Kasr Alainy School of medicine

I. Insulin

- **Action :**

i. Rapid action : **In**sul**in** stimulates **2** things to go **In**to the cells : glucose & K

ii. Gradual action :

1. CHO : *hypoglycemia*
   a. ↑ glycogensis.
   b. ↓ gluconeogenesis.
   c. ↑ peripheral utilization of glucose.
2. fat : - ↑↑ lipogenesis. - ↓↓ lipolysis.
3. protein : anabolic.

- **Preparations :** was discovered in 1921.

Type	Trade names	Duration of action
1- Short-acting : (soluble)	- Neutral (regular). - Humulin R - Semilent.	Onset : < ½ h. Peak : 2 – 4 h. Duration : 6 – 8 h.
2- Intermediate :	- Isophane (NPH) - Humulin N - Lente.	Onset : 2 h. Peak : 6 – 8 h. Duration : 12 – 24 h.
3- Long-acting :	- Protamine zinc insulin - Humulin L - Ultralente	Onset : 6 – 8 h. Peak : 12 – 24 h. Duration : up to 36 h.
4- Insulin mixture :	30% short + 70% NPH **(mixtard)**	

- **Indications :**

i. All type 1 DM.

ii. Type 2 DM not controlled with diet & oral hypoglycemic.

iii. During pregnancy, infection & surgery.

iv. DKA & HHNK .

v. ↑↑ K (Hyperkalemia).

vi. Insulin stimulation test in pan-hpypopituitarism.

- **Dose :** ***trial & error*** (s. c. , 1 cm mixtard = 40 u)

i. Start with 20 – 30 U / d (*20 U in non obese , 30 U in obese patient*)

ii. The dose is gradually ↑ (by 5 u /d) until blood glucose is controlled.

iii. $^2/_3$ of dose before breakfast & $^1/_3$ of dose before lunch.

iv. $^2/_3$ of dose intermediate & $^1/_3$ of dose short acting insulin (***mixtard***)

- If mixtard is not available → 1/3 regular insulin + 2/3 NPH can be mixed in the syringe & injected as rapid as you can.

*- **Multiple SC insulin injection (MSII) :** in cases of poor glycemic control*

- *75% of the dose is given as regular insulin before each meal.*
- *25 % of the dose is given as intermediate insulin before sleep.*

- **Administration :**

i. S.C.

ii. Insulin pump (**C**ontinuous **S**.C **I**nsulin **I**nfusion , CSII) .

iii. IV infusion or IM : in case of DKA , HHNK

iv. Insulin pens.

v. Oral , nasal & rectal insulin → under trial ?

- **Side effects :**

i. Hypoglycemia & hypoglycemic coma.

ii. Allergy : use human insulin.

iii. Insulin resistance :

- obesity → mild resistance.
- antibodies against insulin.

iv. Insulin lipodystrophy : atrophy or hypertrophy of s.c. fat at the site of insulin injections.

v. Insulin edema : Na & H2O retention ⇨ Hypertension.

vi. Weight gain.

vii. Pseudo insulin resistance (*Somogi effect*) : nocturnal hypoglycemia due to over insulin dose at night → ↑↑ anti-insulin hormones → rebound hyperglycemia in the morning. This condition is treated by reduction of the evening insulin dose.

II. TTT of complication : See complications.

Q : criteria for good diabetic control ?

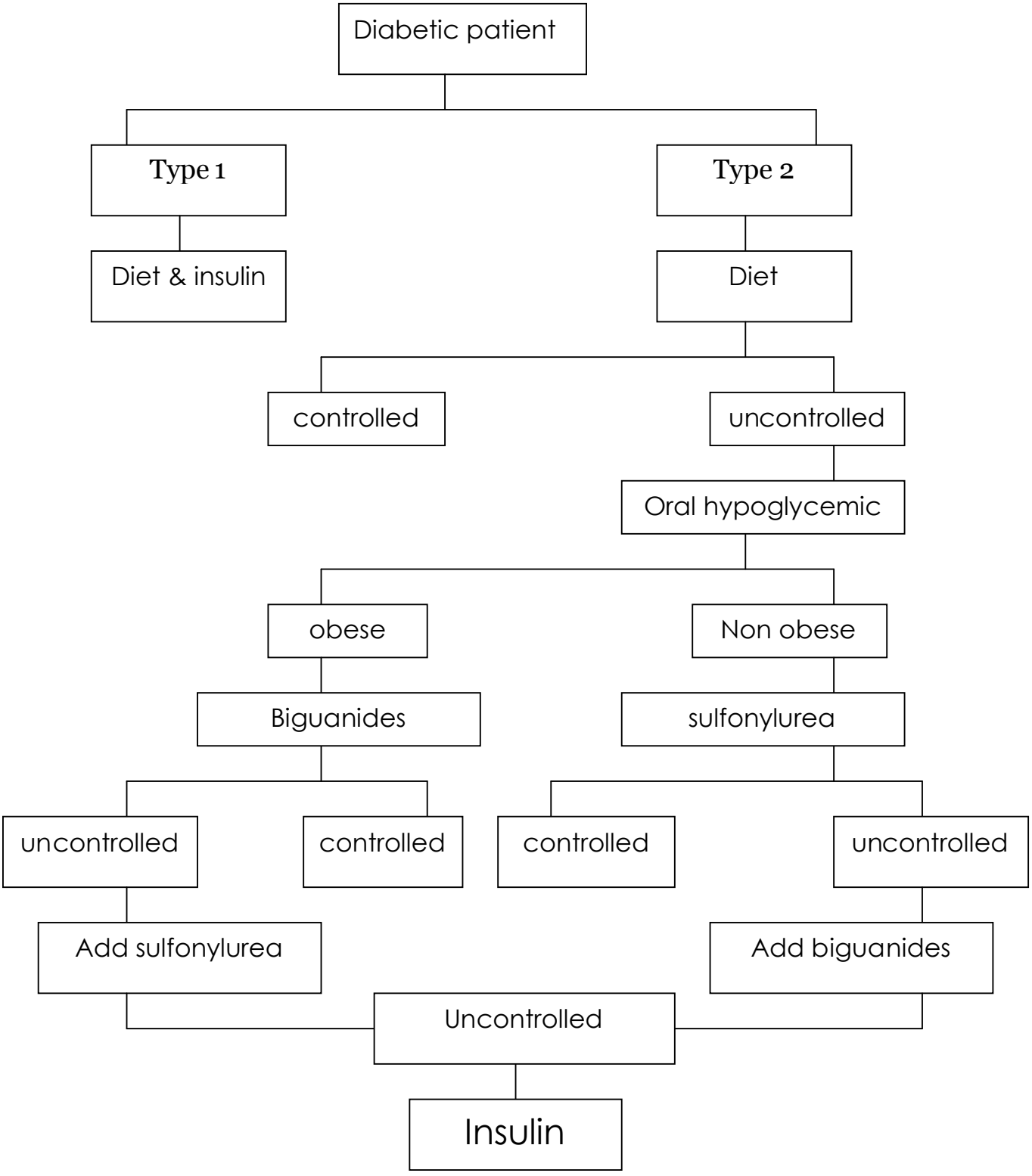
- **Lab. :**
  - Fasting plasma glucose (90 - 130) mg/dl
  - Post prandial plasma glucose : < 180 mg/dl.
  - HbA1c < 7%.
- **Clinical :**
  - No symptoms of DM : .....

Secondary causes of hyperglycemia

I . Hyperglycemia due to tissue insensitivity to insulin :
- Hormonal tumors (acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma)
- Pharmacologic agents (Cortisone, sympathomimetic drugs)
- Liver disease (cirrhosis, hemochromatosis)
- Muscle disorders (myotonic dystrophy)
- Adipose tissue disorders (lipodystrophy, truncal obesity)
- Insulin receptor disorders (acanthosis nigricans syndromes)

II. Hyperglycemia due to reduced insulin secretion :
- Hormonal tumors (somatostatinoma, pheochromocytoma)
- Pancreatic disorders (pancreatitis, hemochromatosis)
- Pharmacologic agents (thiazide diuretics, phenytoin, pentamidine)

Scheme for treatment of DM :



Hypoglycemia

Causes :

I. **Fasting hypoglycemia** :
   - Iatrogenic : insulin , sulfonylureas.
   - Insulinoma : tumor of pancreatic β cell that produce too much insulin.
   - Extrapancreatic tumor(fibrosarcoma , mesothelioma) that produce Insulin like growth factor-I (IGF-1)
   - Starvation.
   - Hepatic dysfunction.
   - Chronic renal failure.
   - Hormonal deficiency : hypopituitarism , hypothyroidism , Addison disease.

II. **Postprandial (reactive) hypoglycemia** :
   - Alimentary hypoglycemia : gastrectomy. this is due to rapid glucose absorption with excessive insulin release ⇨ glucose metabolized rapidly but insulin level remains high resulting in hypoglycemia.
   - Idiopathic type.
   - Early type II DM : The peak value of insulin occur after 2 hours or later when the absorption of CHO from the intestine has been completed.

Clinical picture : see hypoglycemic coma 5 & 5

Investigations :

1- Fasting plasma glucose : < 50 mg% in males , < 45 mg% in females.

2- Plasma level of insulin , thyroxin , cortisol.

3- The insulin / plasma glucose ratio : normally < 0.4 . It is higher in patients with insulinoma.

4- Liver & renal function tests.

5- Abdominal US & CT for tumors.

Treatment :

I. Fasting hypoglycemia :

- The acute attack : see hypoglycemic coma.
- Insulinoma : *MCQ*
  - Surgical removal .
  - Medical to prevent insulin release e.g. diazoxide , octreotide.

II. Postprandial hypoglycemia :

- Diet : Frequent small meals & avoid simple CHO.
- Drugs :
  - **P**robanthine : 7.5 mg 2 h before meals.
  - **P**henytoin : it inhibits insulin secretion.

We think so because all other people think so, or ... because we were told to think so, and think we must think so ...

Rudyard Kipling

Hirsutism

Definition : ↑↑ growth of body hair in androgen dependant areas.

Etiology :

a. Ovarian :
   1. polycystic ovary syndrome > 90% of cases.
   2. ovarian tumors secreting androgens.

b. Adrenal :
   1. congenital adrenal hyperplasia (CAH).
   2. Cushing's syndrome.

c. Drugs :
   - minoxidil.
   - androgens.
   - phenytoin.
   - diazoxide.

Gynaecomastia

Definition:

- Enlargement of the male breast, this is due to a decreased androgens : estrogen ratio.
- It should be differentiated from fatty breast which lacks the glandular element.
- It's unrelated to galactorrhea, breast enlargement is not necessary to make milk.

Etiology : *mnemonic* : **gynecomastia**

- **G**enatic : Klinefelter syndrome
- **Y**oung boy (puberty)
- **N**eonate.
- **E**strogen.
- **C**irrhosis , cimetidine.
- **O**ld age.
- **M**arijuana.
- **A**cromegaly.
- **S**pironolactone.
- **T**umor (testis , adrenal & bronchogenic carcinoma)
- **I**NH.
- **A**lcoholism.

Obesity

Definition :

Obesity is an increase of body adipose (fat tissue) mass.

Etiology :

- Genetic factors.
- Excessive caloric intake.
- Diminished caloric consumption : physical inactivity.
- Endocrinal :
  - Cushing's syndrome.
  - Hypothyroidism.
  - Hypogonadism.
  - Insulinoma.
- Hypothalamic disorders : (DI , polyphagia , obesity , hypersomnia)
- Drugs : Cortisone , Contraceptive pills , Insulin , sulfonylureas , anti-psychotics.

Diagnosis of obesity :

- Body Mass Index (BMI) :

$$\mathrm{BMI} = \frac{weight\ (\mathrm{kg})}{height^2(\mathrm{m}^2)}$$

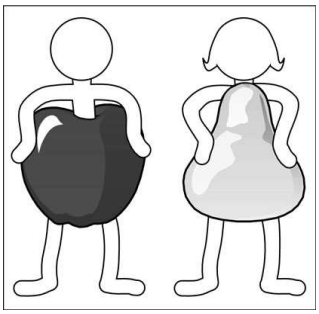
BMI	Classification
18.5 – 25	**normal weight**
25 – 30	overweight
30 – 35	class I obesity
35 – 40	class II obesity
Over 40	class III obesity

- Skin fold thickness e.g. over triceps (N : 20 mm in ♂ , 30 mm in ♀).

- Estimation of body fat : (*Waist / hip ratio*)

a. Central obesity : more fat in the upper body (*Apple shaped*) , associated with more morbidity .

b. Peripheral obesity : more fat in lower body (*pear shaped*) , associated with less morbidity .



Complications : (*Hazards of obesity*)

Cardiovascular :

- Hypertension.
- Atherosclerosis & coronary heart diseases.
- DVT & pulmonary embolism.

Neurological :

- Stroke.
- Migraine.

Endocrinology :

- Type 2 DM.
- Menstrual disorders.

GIT :

- Cholecystitis & gall stones.
- Fatty liver.
- GERD.
- Hernias.

Respiratory :

- Dyspnea (restrictive hypoventilation)
- Sleep apnea syndrome.

Joints :

- Osteoarthritis.
- Back pain.
- Gout.

Psychological : depression & social stigmatization.

Malignancy : Increased incidence of : cancer colon , breast , prostate.

Metabolic syndrome : (*syndrome X*)

- Obesity.
- Hyperlipidemia.
- Hypertension.
- DM.

Treatment :

- Life style & diet modification : Low caloric , balanced diet with mild exercise.
- Drugs :
  - Orlistat (*Xenical*) : inhibits the pancreatic lipase so decrease fat absorption.
  - Sibutramine *(Meridia)* : Appetite suppressant.
- Surgery e.g. Gastric plication , liposuction : indicated with BMI > 40
- Treatment of the cause & complications.

Loss of weight

Etiology :

I. Loss of weight inspite of good appetite :

i. Increased caloric utilization :
   - Thyrotoxicosis.
   - Anexity.
   - Severe exercise.

ii. Decreased intestinal absorption : malabsorption syndrome & diarrhea. (see GIT)

iii. Diabetes mellitus.

iv. Parasitic infection : Ascaris.

II. Loss of weight associated with decreased appetite :

i. Psychological disorders :
   - Depression.
   - Anorexia nervosa.

ii. Gastro-intestinal disorders : e.g.
   - Esophageal diseases.
   - Peptic ulcer.
   - Inflammatory bowel diseases.
   - Hepatobiliary diseases.

iii. Systemic disorders : e.g.
   - Malignancy.
   - Cardiovascular diseases.
   - Infection.

iv. Iatrogenic : Alcohol , Amphetamines : cause appetite suppression leading to weight loss.

v. Smoking.

Endocrinology MCQ

1- Which one of the following inhibits growth hormone secretion from the anterior pituitary gland?

a. Somatostatin.
b. GH releasing hormone.
c. Hypoglycemia.
d. Arginine.
e. Serotonin.

2- In hypertensive individual , which one of the following is the likely finding in a patient with renal artery stenosis and is helpful in distinguishing the condition from Conn's syndrome ?

a. A high aldosterone level
b. A high renin and a high aldosterone level
c. A high renin level
d. A low aldosterone level
e. A low renin and a high aldosterone

3- A 45-year-old obese man without known medical problems complains of feeling very sleepy during the day and often falling asleep while listening to friends. The most likely cause of this patient's problem is

a. narcolepsy
b. upper airway obstruction at night
c. glucocorticoid excess
d. growth hormone excess
e. estrogen excess

4- Obese persons are at an increased risk for which of the following disorders?

a. Hypothyroidism
b. Cholelithiasis
c. Type 1 diabetes mellitus
d. Elevated levels of HDL cholesterol
e. Central sleep apnea

5- Which of the following regimens is best for the preoperative management of a patient with a known pheochromocytoma?

a. Propranolol alone
b. Propranolol followed by phenoxybenzamine
c. Phenoxybenzamine followed by propranolol
d. Prazosin alone
e. Propranolol followed by prazosin

6- Which of the following may be a direct consequence of severe magnesium defciency?

a. Hypophosphatemia
b. Hypercalcemia
c. Hypokalemia
d. Hyponatremia
e. Shortening of the QT interval

7- A 55-year-old woman presents to her physician with mild fatigue. Her past medical history is unremarkable. She is taking no medication. No abnormalities are detected on physical examination. The only abnormality detected on routine blood testing is an elevated calcium (11.9 mg/dL) and a serum inorganic phosphorus of (2 mg/dL). An immunoreactive parathyroid hormone level is undetectable. The most likely etiology for this patient's high serum calcium is

a. primary hyperparathyroidism
b. malignancy
c. hypervitaminosis
d. hyperthyroidism
e. familial hypocalciuric hypercalcemia

8- The most common presentation of primary hyperparathyroidism is

a. bone fracture
b. increased serum creatinine
c. osteitis fibrosa cystica
d. calcium kidney stones
e. asymptomatic hypercalcemia

9- Which of the following medications is known to cause hyperprolactinemia?

a. Metoclopramide
b. Levothyroxine
c. Glucocorticoids
d. Propanolol
e. Cigarette use

10- A 23-year-old woman is diagnosed with Graves'disease shortly after discovering she is pregnant. Appropriate therapy includes

a. radioactive iodine to ablate her thyroid gland
b. propylthiouracil with the goal of maintaining her thyroid function tests in slightly high range.
c. methimazole therapy
d. a beta blocker
e. propylthiouracil with care taken to maintain her thyroid function tests in the mid normal range

11- A 19-year-old man with type 1 diabetes mellitus presents to the emergency room with nausea and vomiting. His arterial pH is 7.16 with potassium of 5.4 mEq/L , bicarbonate of 7 mEq/L, sodium of 132 mEq/L, phosphate of 3.0 mg/dL, and glucose of 475 mg/dL. In addition to intravenous saline & insulin, which electrolyte should be considered in treatment of this case?

a. Bicarbonate
b. Potassium
c. Dextrose
d. Phosphate
e. None of the above

12- The diagnosis of diabetes mellitus is certain in which of the following situations?

a. Abnormal oral glucose tolerance in a 24-year-old woman who has been dieting
b. Successive fasting plasma glucose 147, 165, and 152 mg/dL in an asymptomatic woman
c. A serum glucose level 100 mg/dL in a woman in her twenty-fifth week of gestation after a 50 g oral glucose load
d. Persistent asymptomatic glycosuria in a 30-year-old woman
e. Persistently elevated nonfasting serum glucose levels

13- A 46-year-old woman arrives in your clinic for routine examination. She has no specific complaints, and a full review of systems is unrevealing. On physical examination she has normal vital signs and a 1.5 cm thyroid nodule is palpated in the right lobe of her thyroid; there are no other abnormal findings. A laboratory test reveals a serum TSH level of 2.3 mU/L. Which of the following would be the most appropriate recommendation?

a. Fine-needle aspiration biopsy
b. Unilateral thyroid lobectomy
c. Thyroxine suppressive therapy
d. Radioiodine therapy
e. No intervention needed; a wait and watch approach is recommended

14- Which of the following has been associated with an effective approach towards the prevention of diabetic retinopathy?

a. A reduction in the serum triglyceride level
b. Improved control of blood glucose concentrations
c. Use of an ACE inhibitor
d. Use of aspirin therapy
e. Smoking cessation

15- Which of the following medications is known to cause hypoglycemia?

a. Acetaminophen
b. Pentamidine
c. Epinephrine
d. Verapamil
e. Thiazides

16- Causes of fasting hypoglycemia that are due primarily to <u>overutilization</u> of glucose include

a. acromegaly
b. hepatoma
c. alcohol ingestion
d. congestive heart failure from cor pulmonale
e. Hypopituitarism

17- Manifestations of hypothyroidism include

a. prolongation of the QT interval
b. depressed serum cholesterol
c. microcytic anemia
d. increased serum creatine phosphokinase
e. decreased serum lactate dehydrogenase level

18- Which of the following is most sensitive for detecting diabetic nephropathy?

a. Serum creatinine level
b. Creatinine clearance
c. Urine albumin
d. Glucose tolerance test
e. Ultrasonography

19- **Which of the following statements regarding adrenal insufficiency is true?**

a. The most common cause of adrenal insufficiency is tuberculosis
b. The critical test for the diagnosis of chronic adrenal insufficiency is Synthetic ACTH test
c. Chronic secondary adrenal insufficiency is treated with hydrocortisone and fludrocortisone, whereas chronic primary adrenal insufficiency is treated with hydrocortisone alone
d. ACTH levels greater than normal in secondary adrenal insufficiency.
e. 2ry adrenal insufficiency is characterized by skin pigmentation.

20- **Which of the following statements regarding hyperaldosteronism is true?**

a. The most common causes of secondary hyperaldosteronism are congestive heart failure and cirrhosis with ascites
b. Treatment of primary adrenal hyperaldosteronism is spironolactone
c. Patients with primary adrenal hyperaldosteronism usually present with hypertension, hypokalemia, and metabolic acidosis
d. Diagnosis of primary adrenal hyperaldosteronism is confirmed by elevations in the levels of both renin and aldosterone
e. Patients with primary adrenal hyperaldosteronism usually present with generalized edema.

21- A 42-year-old man with long-standing type 1 diabetes presents with gastroenteritis that has been worsening for 5 days. His blood pressure is 90/55 mm Hg, and his heart rate is 135 beats/min. Other laboratory findings are as follows: blood glucose: 656 mg/dl; sodium: 127 mEq/L; potassium, 4.2 mEq/L; HCO3 : 14 mEq/L; anion gap,25; and pH, 7.05. Which of the following would <u>not</u> be an appropriate step in the immediate treatment of this patient?

a. I.V. administration of 0.9% saline
b. Admission to the intensive care unit
c. I.V. administration of potassium chloride
d. I.V. administration of insulin
e. I.V. administration of sodium bicarbonate

22- **As regard to secondary diabetes, which is correct ?**

a. A patient can be assumed not to be ketosis-prone
b. Most patients with panhypopituitarism are diabetic
c. Classical diabetic complications do not occur
d. Thiazide diuretics and beta-blockers can both impair insulin secretion
e. Most patients with acromegaly are diabetic

23- **The physiological effects of insulin include** .....

a. increased glycolysis
b. increased glycogenolysis
c. increased lipolysis
d. increased gluconeogenesis
e. increased protein catabolism

24- **Sulphonylurea drug therapy in diabetes mellitus** ....

a. causes less weight gain than biguanide therapy
b. increases hepatic gluconeogenesis
c. decreases the number of peripheral insulin receptors
d. decreases hepatic glycogenolysis & gluconeogenesis to reduce hyperglycaemia
e. may be used alone in type 1 DM

25- **Biguanide drug therapy in diabetes mellitus** ....

a. is more likely to cause weight gain
b. Increases plasma immunoreactive insulin concentration
c. Decreases pancreatic glucagon release
d. Inhibits hepatic glycogenolysis
e. Causes troublesome constipation

26- **The clinical features of acromegaly include the following <u>EXCEPT</u> :**

a. Arthropathy & myopathy.
b. Hypertension & impaired glucose tolerance.
c. Goiter & cardiomyopathy.
d. Increased sweating & headache.
e. Skin atrophy & decreased sebum secretion

27- **Typical results of investigations in a patient with acromegaly include :**

a. Failure of the plasma GH to rise during glucose tolerance test
b. Decreased serum prolactin
c. Increased serum IGF-1
d. Abnormality of the pituitary fossa on plain x ray
e. Tumor shrinkage in response octerotide therapy

28 - Which one of the following is true of atrial natriuretic peptide?

a. It causes increased thirst.
b. It causes salt retention.
c. It causes vasodilatation.
d. It is secreted by the juxtaglomerular apparatus.
e. It suppresses the release of aldosterone.

29- Features of multiple endocrine neoplasia (MEN) type 1 include which one of the following ?

a. Adrenal nodules
b. Hyperparathyroidism
c. Hyperthyroidism
d. Hypothyroidism
e. Pheochromocytoma

30 - The most likely etiology for the eating disorder anorexia nervosa is

a. decreased levels of luteinizing hormone– releasing hormone (LHRH)
b. decreased levels of growth hormone
c. decreased levels of insulin-like growth factor I
d. low levels of serum thyroxine
e. psychiatric disorder

31- Which of the following is most likely to be associated with increased insulin sensitivity ?

a. Acromegaly
b. Smoking cessation
c. Pheochromocytoma
d. Polycystic ovary disease
e. Weight loss

32- In metabolic diabetic ketoacidosis (DKA) , the treatment of choice is :

a. Normal saline , IV insulin , metformin.
b. Normal saline , IV insulin , potassium
c. Normal saline , insulin , heparin
d. Normal saline , IV insulin , cortisone
e. IV 5% glucose.

33- In Cushing syndrome which of the following is true ?

a. Esinopenia
b. Basophilia
c. Esinophilia
d. Lymphocytosis
e. Neutropenia

34-The following conditions produce gynecomastia <u>EXCEPT</u> :

a. Digoxin therapy
b. Klinefelter syndrome (XXY syndrome)
c. Bronchogenic carcinoma
d. XYY karyotype
e. Spironolactone therapy

35- Syndrome of inappropriate ADH secretion may result from <u>EXCEPT</u> :

a. Meningitis
b. Bronchial carcinoma
c. Digoxin therapy
d. Head injury
e. Pneumonia

36- Causes of DI include the following <u>EXCEPT</u> :

a. Congenital disorder
b. Craniopharyngioma
c. DIDMOAD syndrome
d. Severe hypocalcemia
e. Sarcoidosis

37- Which of the following test would most reliably defect a deficiency of the GH axis in a 19 year-old man ?

a. ACTH stimulation test
b. Arginine test
c. Glucose test
d. Insulin tolerance test
e. TRH administration test

38 - Causes of nephrogenic DI include the following <u>EXCEPT</u> :

a. Lithium
b. Hypokalemia
c. Congenital disorder
d. Chlorpropamide & carbemazepine therapy
e. Renal amyloidosis

39- A 20 year old lady with a six month history of sweating and diarrhea . She is otherwise well. Her father and grandmother died in middle age but she is unsure of the reason why. On examination, no abnormality could be found. Which one of the following diagnoses would it be important to exclude?

a. Cushing's disease
b. Grave's disease
c. Acromegaly
d. Medullary thyroid carcinoma
e. Premature menopause

40- hypogonadotrophic hypogonadism is typically associated with :

a. Atrophy of the testicular interstitial (Leydig) cells
b. Klinefelter's syndrome (XXY)
c. Isolated GnRH deficiency (*Kallmann's syndrome*)
d. Hemochromatosis
e. Hepatic cirrhosis

41- A patient comes in for a fasting plasma glucose test .On two separate occasion , the result has been 115 and 120 mg/dl which of the following is the most appropriate next step ?

a. Reasurance that these are normal blood sugar
b. Recommend weight loss and exercise.
c. Diagnose DM and start a sulfonylurea agent
d. Recommend cardiac stress test
e. Hospitalize him urgency

42- A 45 year-old obese woman presents for follow up of her diabetes. She currently take glipizide (sulfonylurea) 10 mg twice per day, and her fasting morning glucose is 180 mg/dl. Her last HbA1c was 7.9 . She states that she conscientiously follows her diet and that she walks 45 minutes daily. What is the best next step in her care ?

a. Add an insulin pump
b. Add metformin
c. Add NPH insulin
d. Hospitalize her urgency
e. Add antibiotic

43- The finding of reduced free T4 & TSH is compatible with :

a. Hypopituitarism
b. 1ry hypothyroidism
c. Nephrotic syndrome
d. Pregnancy
e. 2ry hyperthyroidism

44- The following factors are most likely to cause hyperprolactinemia <u>EXCEPT</u> :

a. Breast stimulation
b. Levo dopa
c. Antipsychotics & antiemetics.
d. Renal failure
e. hypothyroidism

45- A 33-year old woman is noted to have Grave's disease .Which of the following is the best therapy ?

a. Long term propranolol.
b. Lifelong oral propylthiouracil (PTU)
c. Radioactive iodine ablation
d. Surgical thyroidectomy
e. Lifelong SC insulin

46- The clinical features of thyrotoxicosis include the following <u>EXCEPT</u> :

a. atrial fibrillation
b. weight loss & amenorrhea
c. proximal myopathy
d. exophthalmos
e. decreased insulin requriments in type 1 DM

47- Causes of hypercalcemia include <u>EXCEPT</u>

a. bone metastases
b. carcinomas secreting PTH like peptides
c. Addison's disease
d. severe hypothyroidism
e. chronic sarcoidosis

48- In 1ry hyperaldosteronism (Conn's syndrome) ...

a. peripheral edema is usually present
b. proximal myopathy is due to hypokalemia
c. severe hypertension is characteristic
d. DM is often present
e. hypertension is associated with hyperreninemia

49- Which one of the following is characteristic of insulin resistance ?

a. acanthosis nigricans
b. nephropathy
c. retinopathy
d. hypoglycemia
e. peripheral neuropathy

50 – In diabetic patient , clinical feature suggesting hypoglycemic coma rather than DKA include ...

a. systemic hypotension
b. air hunger
c. abdominal pain
d. moist skin & tongue
e. hyporeflexia

Answers

1- a) somatostatin.
GHRH , Hypoglycemia , insulin , arginine , serotonin → ↑GH.

2- c) A high renin level
Renal artery stenosis results in high renin and high aldosterone levels in contrast to Conn's syndrome in which the aldosterone level is high but the renin is characterisitically suppressed.

3-b) upper airway obstruction at night.
Grossly obese patients are more likely than are the nonobese to have high blood pressure, peripheral vascular disease, cerebrovascular disease, diabetes, and hyperlipidemia. The so-called Pickwickian syndrome, which is characterized by hypersomnolence during the day, is thought to be due to nocturnal upper airway obstruction that leads to hypoxemia and hypercapnia and causes arousal with each episode.This chronic arousal pattern at night causes sleep deprivation and daytime somnolence. Hyperinsulinemia, insulin resistance, diabetes, and hyperlipidemia may all be more common in obese persons but are not believed to play a role in the obesity-hypoventilation syndrome or in daytime somnolence.

4- b) Cholelithiasis

5- c) Phenoxybenzamine followed by propranolol
Pheochromocytomas produce and secrete catecholamines, which may lead to paroxysmally high blood pressure. It is important to prepare the patient for surgery by preventing the effects of catecholamine release through treatment with phenoxybenzamine, a long-acting-adrenergic blocker. Beta blockers should not be given before alpha blockade has been established because of the potential for hypertension as aresult of the antagonism of beta-mediated vasodilation in skeletal muscle beds. However, propranolol is useful in treating the reflex tachycardia induced by phenoxybenzamine. While prazosin is an effective agent for the treatment of hypertensive crises associated with pheochromocytoma, its use as a primary agent in the management of this disorder has not been established.

6- c) Hypokalemia
About half of patients with hypomagnesemia may become hypokalemic (the mechanism is unclear, but secondary hyperaldosteronism may play a role). This hypokalemia is refractory . Hyponatremia is not a known consequence of hypomagnesemia. Because of QT prolongation, dangerous arrhythmias are more likely to occur.

7- b) malignancy.
hypercalcemia and hypophosphatemia without elevated levels of PTH are likely to have the hypercalcemia of malignancy. Patients with excessive levels of vitamin D would not be expected to have a low serum phosphate. Second, patients with familial hypocalciuric hypercalcemia, an autosomal dominant trait, often have normal or slightly low levels of immunoreactive parathyroid hormone. It is now clearly recognized that many solid tumors, including carcinomas of the lung and kidney, may produce (PTH like) that will not be identified by the currently available assays that detect true parathyroid hormone elaborated from the parathyroid gland.

8- e) Asymptomatic hypercalcemia.

At present, this is the most common source of diagnoses of hyperparathyroidism. A solitary parathyroid adenoma is the most common cause of asymptomatic hypercalcemia.

9- a) Metoclopramide

Medications are important causes of hyperprolactinemia include dopamine-blocking drugs (e.g., phenothiazines, , metoclopramide, methyldopa and reserpine)

10- b) propylthiouracil therapy with the goal of maintaining her thyroid function tests in the high-normal or slightly high range.

Radioactive iodine should never be given to a pregnant woman. In addition, both methimazole and beta blockers should be avoided in pregnant women. Antithyroid drugs, including propylthiouracil, cross the placenta and affect fetal thyroid function Studies have shown that when a treated pregnant woman's thyroid function is in the mid-normal range, the fetus is hypothyroid. When the mother's thyroid tests are maintained in the high-normal or slightly hyperthyroid range, the fetus is likely to have normal thyroid function.

11- b) potassium.

The mainstay of therapy for diabetic ketoacidosis (DKA) is insulin and intravenous fluids. DKA cannot be reversed without insulin. Although the serum K concentration is high,. The K concentration will drop quickly due to insulin therapy (due to intracellular shift) .

Because glucose levels drop more quickly than ketones disappear from the plasma, it is usually necessary to give intravenous dextrose when the blood glucose level drops below about (250 to 300 mg/dL). This allows continued administration of insulin to clear the ketones from the blood..

Bicarbonate therapy is not recommended unless the arterial pH falls below 7.10 or 7.00 because the rapid alkalinization may impair oxygen delivery to tissues and impair left ventricular function. In addition, insulin therapy is effective in reversing the acidemia without the assistance of bicarbonate therapy.

12- b) Successive fasting plasma glucose 147, 165, and 152 mg/dL in an asymptomatic woman

persistent fasting hyperglycemia even if it is asymptomatic, has been recommended by the National Diabetes Data Group as a criterion for the diagnosis of diabetes.

Abnormal glucose tolerance—whether after eating or after a standard "glucose tolerance test"—can be caused by many factors (e.g., anxiety, infection or other illness) Similarly, glycosuria may have renal as well as endocrinologic causes. Therefore, these two conditions cannot be considered diagnostic of diabetes. Gestational diabetes is diagnosed in women between the 24 – 28 weeks of gestation, first using a 50-g oral glucose load , if the 1-h glucose level 140 mg/dL; a 100-g oral glucose test is performed after an overnight fast. Gestational diabetes is initially treated with dietary measures; if the postprandial glucose level remains elevated, insulin therapy is often started. About 30% of women with gestational diabetes will eventually develop true DM.

13- a) Fine-needle aspiration biopsy

Fine-needle aspiration biopsy is indicated in all patients with solitary thyroid nodules. Approximately 5% of all solitary thyroid nodules are thyroid carcinomas.

14- b) Improved control of blood glucose concentrations.

Improved glycemic control produced a remarkable reduction in the rate of the development of retinopathy. **It should be noted that better control of hyperglycemia lowers but does not eliminate the risk of retinopathy and other complications of diabetes mellitus.**

15– b) Pentamidine (Antiprotozoal)
Insulin, sulfonylureas, disopyramide, and pentamidine all cause hypoglycemia through hyperinsulinemia. Thiazides can cause hyperglycemia.Beta agonists (e.g. epinephrine) and calcium channel blockers have no effect on serum glucose levels. Acetaminophen when taken in normal dosages does not affect the serum glucose concentration; however, an overdose causing hepatic damage could lead to severe hypoglycemia.

16- b) Hepatoma

17- d) increased serum creatine phosphokinase
Decreased QRS amplitude on ECG is common. Elevated creatine phosphokinase and lactic dehydrogenase serum values may mimic a myocardial infarction. Hypothyroidism also is typically associated with macrocytic anemia caused by coexistent pernicious anemia or unknown factors. Serum cholesterol is elevated in many patients with primary hypothyroidism.

18- c) urine albumin.
Diabetic nephropathy may be functionally silent for 10 to 15 years. Clinically detectable diabetic nephropathy begins with the development of microalbuminuria (30 to 300 mg of albumin /day). The glomerular filtration rate actually may be elevated at this stage. Only after the passage of additional time will the proteinuria be overt enough (0.5 g/L) to be detectable on standard urine dipsticks. Microalbuminuria precedes nephropathy in patients with both type 1 & 2 DM. An increase in kidney size also may accompany the initial hyperfiltration stage. Once the proteinuria becomes significant enough to be detected by dipstick, a steady decline in renal function occurs, with the glomerular filtration rate falling an average of 1 mL per minute per month.Hypertension clearly is exacerbating factor for diabetic nephropathy.

19-b) The critical test for the diagnosis of chronic adrenal insufficiency is Synthetic ACTH test
autoimmune adrenal destruction is the most common cause. The critical test for the diagnosis of chronic adrenal insufficiency is the synthetic ACTH stimulation test. Synthetic ACTH is administered in a 250 μg intravenous bolus, and plasma cortisol levels are measured 30 and 60 minutes afterward. Values greater than 20 μg/dl exclude 1ry adrenal insufficiency. The differential diagnosis of adrenal insufficiency requires the discrimination of primary and secondary causes. The most useful test for this is measurement of the ACTH level. ACTH levels greater than normal in primary disease; below than normal in secondary disease. Primary chronic adrenal insufficiency is treated with oral hydrocortisone & Fludrocortisone (aldosterone). Chronic secondary adrenal insufficiency is treated in the same way as chronic primary disease but with replacement of hydrocortisone only, not aldosterone.

20 a) The most common causes of secondary hyperaldosteronism are congestive heart failure and cirrhosis with ascites
Primary hyperaldosteronism is caused by benign adrenal adenomas, which are typically unilateral and are usually less than 2.5 cm in diameter. Patients present with mild hypertension without edema due to renal escape phenomenon. Laboratory testing shows hypernatremia , hypokalemia and metabolic alkalosis not acidosis. Diagnosis is confirmed by elevated plasma aldosterone levels (> 14 ng/dl) & suppressed plasma renin activity .The treatment of primary hyperaldosteronism is unilateral adrenalectomy, preferably by a laparoscopic procedure. Secondary hyperaldosteronism may or may not be associated with hypertension.

21- e) I.V. administration of sodium bicarbonate
Administration of bicarbonate is not generally required in most cases of DKA and is generally reserved for treatment of severe acidosis (pH < 7.0 or HCO_3 < 10)

22- d) Thiazide diuretics and beta-blockers can both impair insulin secretion
Secondary diabetes causes all the same complications as primary diabetes, including DKA. 15% of patients with acromegaly are diabetic

23- a) increased glycolysis

24- d) decreases hepatic glycogenolysis & gluconeogenesis to reduce hyperglycaemia

25- d) Inhibits hepatic glycogenolysis
Biguanide is more likely to cause weight loss than weight gain. There is no increases of plasma immunoreactive insulin concentration , hence does not cause hypoglycaemia in non-diabetics. Biguanide causes diarrhea which may limit drug compliance.

26- e) skin atrophy & decreased sebum secretion.

27- c) Increased serum IGF-1
GH normally falls during the glucose tolerance test. Increased serum prolactin occurs in 30%. Octerotide reduces GH secretion but not tumor size.

28- c) It causes vasodilatation
Atrial natriuretic peptide is a peptide hormone secreted from the myocardium & causes natriuresis (excretion of Na) .It is released under conditions of hypervolemia (myocardial stretch) and its actions are : ↓ thirst , vasodilatation & excretion of Na . It acts directly on the kidney rather than via suppression of aldosterone.

29- b) Hyperparathyroidism
MEN type 1 : Hyperparathyroidism , pituitary tumor & pancreatic tumor (insulinoma)
MEN type 2 : Hyperparathyroidism , medullary thyroid cancer & pheochromocytoma.

30- e) psychiatric disorder
The disease usually begins shortly after puberty and is characterized by profound weight loss caused by a lack of caloric intake and a high level of physical activity. Other features include cold intolerance caused by a secondary defect in regulatory thermogenesis, hypothalamic amenorrhea, hypokalemia, low serum immunoglobulins, normal or elevated growth hormone levels, decreased levels of IGF 1 , and low serum T3 concentrations. All these abnormalities seem to result from, rather than cause, the eating disorder. Most authorities favor a psychiatric etiology. Unfortunately, the benefits of psychiatric intervention and behavior modification have been somewhat marginal. Hospitalization may be required to save the patient's life if the anorexia nervosa is severe.

31- e) weight loss

32- b) Normal saline , IV insulin , potassium.

33- a) Esinopenia
Cortisone increases RBCs , Neutophils & decreases esinophilis , lymphocytes , basophilis.

34- d) XYY karyotype.

35- c) digoxin therapy.

36- d) severe hypocalcemia.

37-d) insulin tolerance test.

38- d) Chlorpropamide & carbemazepine therapy

39- d) Medullary thyroid carcinoma

Medullary thyroid carcinoma (MTC) can secrete a variety of peptides and prostaglandins , resulting in extra-thyroid symptoms. Diarrhea and sweating are the most common. It is an important tumor to exclude since it can metastasise early. MTC can be inherited as part of MEN type 2 .

Acromegaly can also cause sweating due to sweat gland hypertrophy , but usually not diarrhea. Cushing's disease also rarely presents with these symptoms. Both these conditions also rarely show such strong family history

40- c) Isolated GnRH deficiency (*Kallmann's syndrome*)

In a case of Atrophy of the testicular interstitial (Leydig) cells , serum LH is elevated.

In Klinefelter's syndrome , serum FSH is elevated.

Hemochromatosis : testicular damage with hypergonadotrophic.

41- b) Recommend weight loss and exercise.

By diagnostic criteria ,this patient falls into the definition of impaired fasting glucose (pre diabetes). Although he does not yet meet the criteria for diabetes , he is at greater risk for developing diabetes in the future and for macrovascular disease. Intervention such as weight loss will decrease his insulin resistance , and following a diet lower in simple sugar and fats may place less stress on his pancreas and increase the time to development of diabetes.

42- b) Add metformin

Because this patient is obese & young type 2 diabetic . Insulin may be associated with weight gain ,and most patients prefer to be maintained on oral agents rather than injections, if possible

43- a) Hypopituitarism

44- b) levo dopa

45- c) Radioactive iodine ablation

It is the definitive treatment for Grave's disease. Surgery is indicated for obstructive symptoms or for women during pregnancy.

46- e) decreased insulin requirements in type 1 DM.

47- d) severe hypothyroidism

48- b) proximal myopathy is due to hypokalemia.

49- a) acanthosis nigricans.

50- d) moist skin & tongue.

Collections of endocrine

Endocrinal emergencies :

a. Diabetic comas.
b. **Thyroid emergencies** :
    i. Thyrotoxic crisis.
    ii. Myxoedema coma.
c. Parathyroid emergencies :
    i. Acute hypercalcemia.
    ii. Tetany.
d. Addisonian crisis.

Endocrinal manifestations of systemic diseases :

a. **Liver cell failure** : (↑ ADH & ↑ aldosterone)
    i. In ♂ : gynecomastia , ♀ pubic hair , ↓ libido.
    ii. In ♀ : breast atrophy , ♂ pubic hair , ↓ libido.
b. **Chronic renal failure** :
    i. 2ry & 3ry hyperparathyroidism.
    ii. Hyperprolactinemia.
c. **T.B. (miliary)** : Addison's disease.
d. **Heamochromatosis** :
    i. DM.
    ii. Hypogonadism.
e. **Sarcoidosis** :
    i. DI.
    ii. Addison's disease.
f. **Malabsorption**: 2ry hyperparathyroidism.
g. **Bronchogenic carcinoma,Hepatoma& hypernephroma** :
    Endocrinal manifestations of paramalignant syndrome.

Endocrinal causes of HTN :

a. Pituitary : acromegaly.
b. Thyroid : - hypothyroidism → ↑ diastolic Bl.P.
    - hyperthyroidism → ↑ systolic Bl.P.
c. Parathyroid : hyperparathyroidism.
d. Pancreas : DM.
e. Suprarenal : Conn's , Cushing syndrome, Pheochromocytoma.

Endocrinal causes of hyperlipidemia :

a. Hypothyroidism.
b. DM.
c. Obesity.

Endocrinal causes of osteoprosis :

a. DM.
b. Hyperthyroidism.
c. Hyperparathyroidism.
d. Cushing syndrome.
e. Osteomalacia.

Macro & micro-vascular complications of DM :

a. Macro :
    i. HTN.
    ii. Atherosclerosis.
    iii. Non healing ulcers & amputations.
b. Micro : (Triopathy)
    i. Retinopathy.
    ii. Nephropathy.
    iii. Neuropathy.

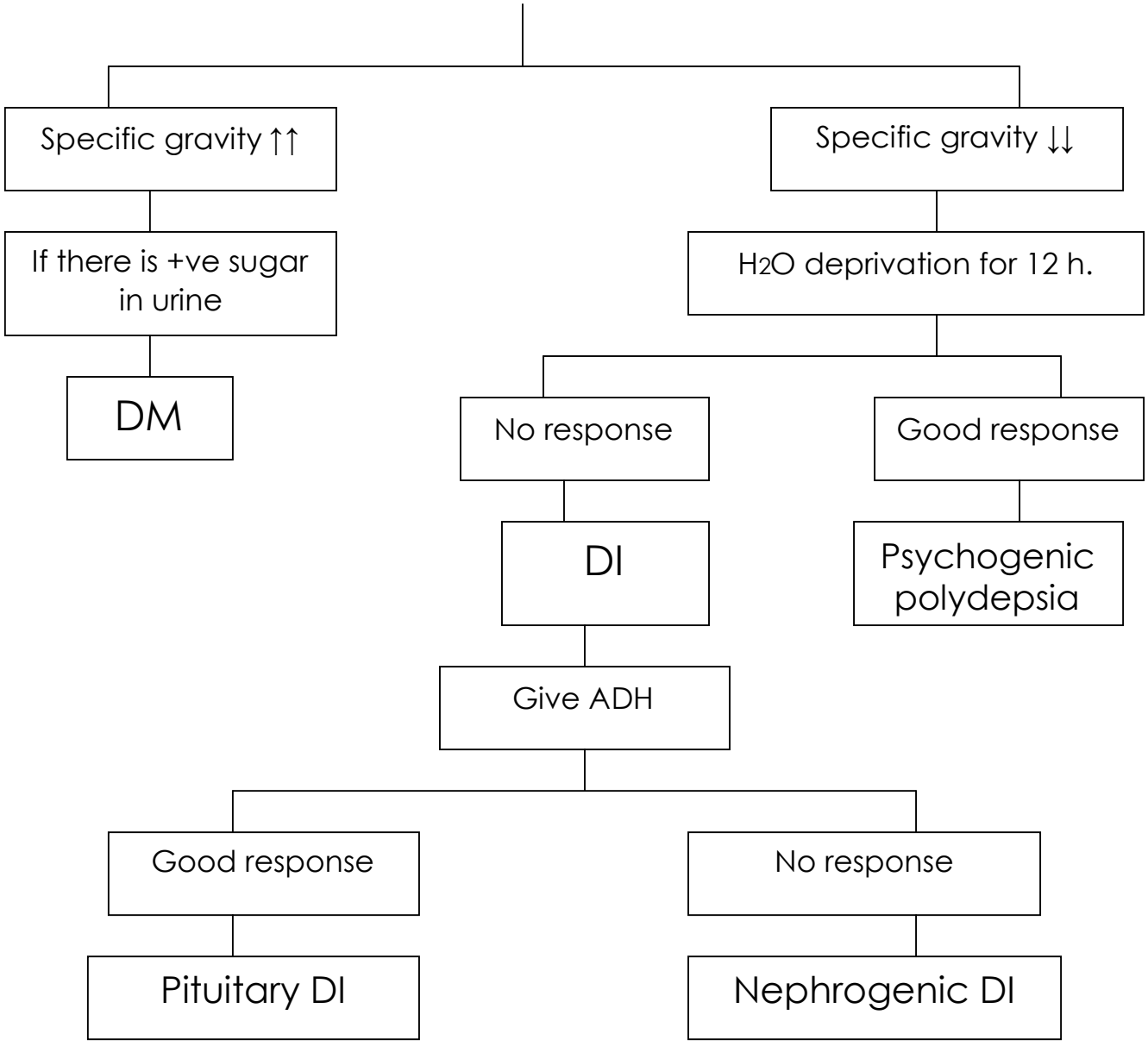
Immune mediated endocrinal diseases :

a. Type 1 DM.
b. Addison's disease.
c. Grave's disease, Hashimoto thyroditis.

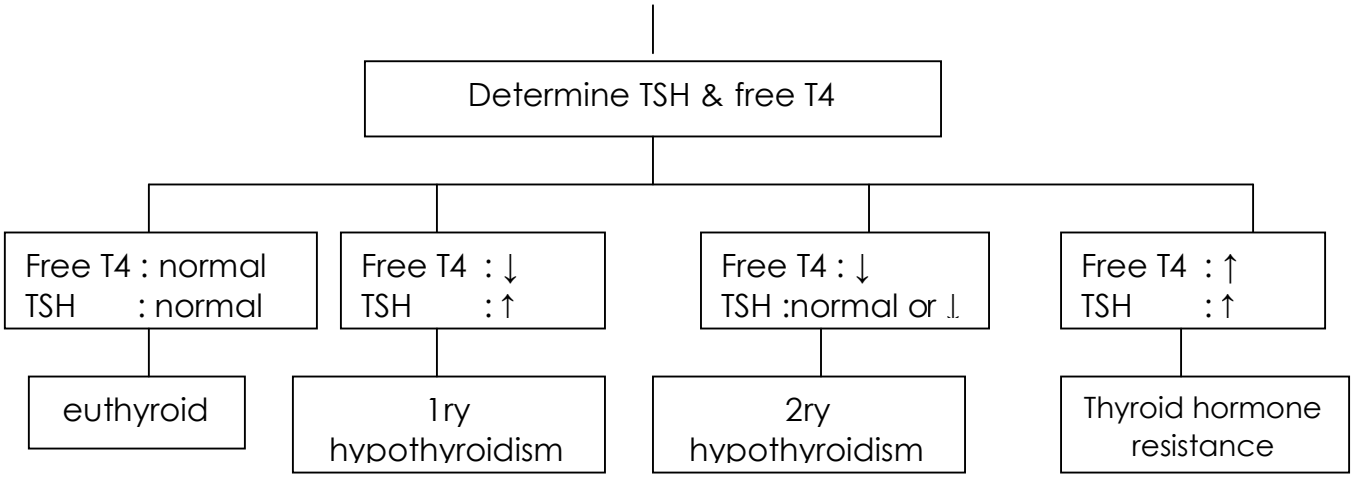
Iatrogenic endocrinal diseases :

- Iodine → hyperthyroidism.
- Lithium → hypothyroidism.
- Amiodarone → thyroid dysfunction.
- Ketoconazole → hyoadrenalism.
- Metoclopramide → Hyperprolactinaemia.
- Sympathomimetic → picture like thyrotoxicosis.
- ACE s inhibitors → hypoldosteronism.
- Steroid therapy → DM & Cushing syndrome.
- Thyroxin therapy → thyrotoxicosis (factitious).
- Vitamin D → hypercalcemia.
- Insulin & oral hypoglycemic → hypoglycemia.

Approach to patient with polyuria & polydepsia :



Approach to patient with hypothyroidism :



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